

WEST Search History

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DATE: Wednesday, June 06, 2007

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=PGPB,USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L1	((mitiglinide) near12 (diabetic or diabetes or postprandial or glycemia or glucose or complication or hypoglycemia))	26

END OF SEARCH HISTORY

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	282	mitiglinide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:15
S2	19	S1 AND @pd<"20030606"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/05/21 16:36
S3	282	mitiglinide or mitiglinide or mitglinide or mitiglnde or mitiginide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:11
S4	24	S3 near11 (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:14
S5	275	S3 and (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:13
S6	184	S3 same (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/23 08:13
S7	142	S3 with (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55

EAST Search History

S8	285	mitiglinide or mitiglinide or mitglinide or mitiglnde or mitiginide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S9	143	S8 with (diabet\$ OR Diabetic OR diabetes or complication or glycemic or glucose)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S10	143	S9	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S11	751036	mitiglinide calcium hydrate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 10:55
S13	28	mitiglinide calcium hydrate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2007/05/24 10:56

EAST Search History

S14	99	("20050267195" "20050215607" ."6365176" "6251926" "20030040490" "20070072813" "6277877" "5981488" "6380223" "5932258" "20060188443" "4360019" "20050272640" "6268343" "6372244" "20050203001" "6376549" "6432993" "6143786" "6355635" "6287586" "6461870" "6458378" "6835400" "7183266" "20030012807" "20030017191" "20030125301" "20040185129" "5523087" "20060122244" "5597893" "6316429" "5919216" "20020193344" "20060257987" "20070037812" "20070066683" "20070082907" "6294538" "6362009" "6414149" "6414126" "6221633" "6221633" "6251905" "6297269" "6677358" "6316489" "6369075").pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:17
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S16	128	S14 or S15	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:59

EAST Search History

S17	285	mitiglinide	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:59
S18	121	S16 NOT S17	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/24 11:59
S19	569	(514/412).CCLS.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/05/25 11:25
S20	829	(514/310).CCLS.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/05/25 11:25
S21	1492	(514/563).CCLS.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/05/25 11:25
S22	2872	S19 or S20 or S21	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:26
S23	2243	S22 and @pd<"20050930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:29

EAST Search History

S24	1868	S22 and @pd<"20040930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:29
S25	349	S19 and @pd<"20040930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 11:30
S26	683	(S20 or S21) and diabetes	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:46
S27	794	(S20 or S21) and diabet\$	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:47
S28	399	S27 and @pd<"20040930"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:49
S29	792	S27 not S25	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:49
S30	792	S27 NOT S25	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/25 12:49

EAST Search History

S31	1658	MIKOSHIBA.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:32
S32	309100	SUZUKI.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:32
S33	460206	SUZUKI, HISAO.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:32
S34	542	SUZUKI near HISAO.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:33
S36	26	KIYONO near YUJI.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:33
S38	2213	S31 or S34 or S36	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:34
S39	12	S38 and diabetes	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/05/31 11:34

EAST Search History

S40	7	S38 and diabetes	USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2007/05/31 11:34
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ANSWER SUMMARY

L2 ANSWER 1 OF 1416 CAPLUS

Voltage regulator [machine translation]; 2007:536206 CAPLUS

L2 ANSWER 2 OF 1416 CAPLUS

An optical drive having a laser driver device with an adjustable power level; 2007:512519 CAPLUS

L2 ANSWER 3 OF 1416 CAPLUS

PCR detection of Reg IV mRNA for cancer diagnosis; 2007:485237 CAPLUS

L2 ANSWER 4 OF 1416 CAPLUS

2-Propenoic acid, methyl ester, polymer with ethenyl acetate, hydrolyzed, sodium salts; tolerance exemption; 2007:473041 CAPLUS

L2 ANSWER 5 OF 1416 CAPLUS

Roles of CD4+CD25+ T cells in the development of experimental murine allergic conjunctivitis; 2007:471425 CAPLUS

L1 ANSWER 1 OF 90 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L3 ANSWER 1 OF 4 REGISTRY

(α S,3aR,7aS)- octahydro- γ -oxo- α -(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 1 OF 4 REGISTRY

(α S,3aR,7aS)- octahydro- γ -oxo- α -(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 2 OF 4 REGISTRY

(α S,3aR,7aS)- octahydro- γ -oxo- α -(phenylmethyl)-2H-Isoindole-2-butanoic acid; 145375-43-5 REGISTRY

L3 ANSWER 3 OF 4 REGISTRY

hydrochloride (1:2) 4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-Piperazineethanol; 146-56-5 REGISTRY

L3 ANSWER 4 OF 4 REGISTRY

4-chloro- α -(4-chlorophenyl)- α -(trichloromethyl)- Benzenemethanol; 115-32-2 REGISTRY

L7 ANSWER 1 OF 85 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L7 ANSWER 2 OF 85 CAPLUS

Carboxyl-glucuronidation of mitiglinide by human UDP-glucuronosyltransferases; 2007:453224 CAPLUS

L7 ANSWER 3 OF 85 CAPLUS

Mitglinide and α -glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L7 ANSWER 4 OF 85 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L7 ANSWER 5 OF 85 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L4 ANSWER 1 OF 6 CAPLUS

Characterization of the action of S 21403 (mitiglinide) on insulin secretion and biosynthesis in normal and diabetic β -cells; 2005:1205798 CAPLUS

L4 ANSWER 2 OF 6 CAPLUS

Pharmacological and clinical profile of mitiglinide calcium hydrate (Glufast), a new insulinotropic agent with rapid onset; 2004:836630 CAPLUS

L4 ANSWER 3 OF 6 CAPLUS

Rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride; 2004:496322 CAPLUS

L4 ANSWER 4 OF 6 CAPLUS

Rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostpradial hyperglycemic agent: comparison with nateglinide; 2004:345396 CAPLUS

L4 ANSWER 5 OF 6 CAPLUS

Characterization of hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel hypoglycemic agent: comparison with glibenclamide, a sulfonylurea; 2004:345395 CAPLUS

L4 ANSWER 6 OF 6 CAPLUS

Effects of S 21403 on hormone secretion from isolated rat pancreas at different glucose concentrations; 2002:894053 CAPLUS

L1 ANSWER 1 OF 2 REGISTRY

(α S,3aR,7aS)- octahydro- γ -oxo- α -(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 1 OF 129 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L3 ANSWER 2 OF 129 CAPLUS

Mitglinide and α -glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L3 ANSWER 3 OF 129 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L3 ANSWER 4 OF 129 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L3 ANSWER 5 OF 129 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287142 CAPLUS

L3 ANSWER 6 OF 129 CAPLUS

Study on environmental risk assessment of drugs: excretion forms to environment; 2007:276713 CAPLUS

L3 ANSWER 7 OF 129 CAPLUS

High-performance liquid chromatography-electrospray ionization mass spectrometry determination of Mitiglinide in human plasma and its pharmacokinetics; 2007:207390 CAPLUS

L3 ANSWER 8 OF 129 CAPLUS

Sulfonylureas and glinides exhibit peroxisome proliferator-activated receptor γ activity: a combined virtual screening and biological assay approach; 2007:141807 CAPLUS

L3 ANSWER 9 OF 129 CAPLUS

Potassium channel blockers for treatment of migraine and headache; 2007:88262 CAPLUS

L3 ANSWER 10 OF 129 CAPLUS

Preparation of N-terminally modified GLP-1 receptor modulators and their use in the

treatment of diabetes and related conditions; 2006:1253322 CAPLUS

L5 ANSWER 1 OF 91 CAPLUS

Long-term effect of combination therapy with mitiglinide and once daily insulin glargine in patients who were successfully switched from intensive insulin therapy in short-term study; 2007:548465 CAPLUS

L5 ANSWER 2 OF 91 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L5 ANSWER 3 OF 91 CAPLUS

Carboxyl-glucuronidation of mitiglinide by human UDP-glucuronosyltransferases; 2007:453224 CAPLUS

L5 ANSWER 4 OF 91 CAPLUS

Mitglinide and α -glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L5 ANSWER 5 OF 91 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L5 ANSWER 6 OF 91 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L5 ANSWER 7 OF 91 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287142 CAPLUS

L5 ANSWER 8 OF 91 CAPLUS

Sulfonylureas and glinides exhibit peroxisome proliferator-activated receptor γ activity: a combined virtual screening and biological assay approach; 2007:141807 CAPLUS

L5 ANSWER 9 OF 91 CAPLUS

Preparation of N-terminally modified GLP-1 receptor modulators and their use in the treatment of diabetes and related conditions; 2006:1253322 CAPLUS

L5 ANSWER 10 OF 91 CAPLUS

Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes; 2006:1252442 CAPLUS

L5 ANSWER 11 OF 91 CAPLUS

Combined pharmaceutical preparation for treatment of type 2 diabetes; 2006:1157536 CAPLUS

L5 ANSWER 12 OF 91 CAPLUS

Imaging docking and fusion of insulin granules induced by antidiabetes agents. Sulfonylurea and glinide drugs preferentially mediate the fusion of newcomer, but not previously docked, insulin granules; 2006:1056090 CAPLUS

L5 ANSWER 13 OF 91 CAPLUS

Process for preparation of isoindoline derivatives as antidiabetic agents; 2006:969655 CAPLUS

L5 ANSWER 14 OF 91 CAPLUS

Roflumilast for the treatment of diabetes mellitus; 2006:945768 CAPLUS

L5 ANSWER 15 OF 91 CAPLUS

Roflumilast for the treatment of diabetes mellitus and accompanying disorders, and combinations with other agents; 2006:944442 CAPLUS

L5 ANSWER 16 OF 91 CAPLUS

Effects of mitiglinide on glucose -induced insulin release into the portal vein and fat-induced triglyceride elevation in prediabetic and diabetic OLETF rats. [Erratum to document cited in CA145:262963]; 2006:898535 CAPLUS

L5 ANSWER 17 OF 91 CAPLUS

Manufacture and application of drug composition containing pioglitazone hydrochloride and mitiglinide for treating insulin-dependent diabetes mellitus; 2006:840773 CAPLUS

L5 ANSWER 18 OF 91 CAPLUS

Manufacture of dripping pill containing mitiglinide for treating diabetes mellitus; 2006:840772 CAPLUS

L5 ANSWER 19 OF 91 CAPLUS

Medicinal compositions containing hypoglycemic agents; 2006:766544 CAPLUS

L5 ANSWER 20 OF 91 CAPLUS

Manufacture of mitiglinide enteric-coated preparation; 2006:666684 CAPLUS

L5 ANSWER 21 OF 91 CAPLUS

Effects of mitiglinide on glucose -induced insulin release into the portal vein and fat-induced triglyceride elevation in prediabetic and diabetic OLETF rats; 2006:664881 CAPLUS

L5 ANSWER 22 OF 91 CAPLUS

Mitiglinide sustained-release preparation and its production method; 2006:519723 CAPLUS

L5 ANSWER 23 OF 91 CAPLUS

Therapeutic efficacy of mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargin in patients with type 2 diabetes mellitus; 2006:505268 CAPLUS

L5 ANSWER 24 OF 91 CAPLUS

Synthesis and hypoglycemic activity of mitiglinide analogs; 2006:328612 CAPLUS

L5 ANSWER 25 OF 91 CAPLUS

Mitiglinide oral preparations for the treatment of diabetes; 2006:220560 CAPLUS

L5 ANSWER 26 OF 91 CAPLUS

Rapid insulin secretagogue: Mitiglinide; 2006:64372 CAPLUS

L5 ANSWER 27 OF 91 CAPLUS

Manufacture of compound hypoglycemic drug containing mitiglinide and metformin hydrochloride; 2006:39395 CAPLUS

L5 ANSWER 28 OF 91 CAPLUS

Pharmaceutical composition for prevention or treatment of lipid metabolism disorder; 2005:1220708 CAPLUS

L5 ANSWER 29 OF 91 CAPLUS

Characterization of the action of S 21403 (mitiglinide) on insulin secretion and biosynthesis in normal and diabetic β -cells; 2005:1205798 CAPLUS

L5 ANSWER 30 OF 91 CAPLUS

Effects of S21403 (mitiglinide) on postprandial generation of oxidative stress and inflammation in type 2 diabetic patients; 2005:1009580 CAPLUS

L5 ANSWER 31 OF 91 CAPLUS

Method for examining blood glucose control state; 2005:962511 CAPLUS

L5 ANSWER 32 OF 91 CAPLUS

Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases; 2005:120729 CAPLUS

L5 ANSWER 33 OF 91 CAPLUS

Rapid acting insulin secretagogue in treatment for type 2 diabetes; 2005:43407 CAPLUS

L5 ANSWER 34 OF 91 CAPLUS

The impact of ATP-sensitive K⁺ channel subtype selectivity of insulin secretagogues for the coronary vasculature and the myocardium; 2004:1076146 CAPLUS

L5 ANSWER 35 OF 91 CAPLUS

Mitiglinide calcium dihydrate; 2004:1072015 CAPLUS

L5 ANSWER 36 OF 91 CAPLUS

Synthesis of antidiabetic mitiglinide calcium hydrate; 2004:1070406 CAPLUS

L5 ANSWER 37 OF 91 CAPLUS

A synergistic pharmaceutical combination comprising cicletanine for the prevention or treatment of diabetes; 2004:902180 CAPLUS

L5 ANSWER 38 OF 91 CAPLUS

Pharmacological and clinical profile of mitiglinide calcium hydrate (Glufast), a new insulinotropic agent with rapid onset; 2004:836630 CAPLUS

L5 ANSWER 39 OF 91 CAPLUS

Remedy for diabetes; 2004:681582 CAPLUS

L5 ANSWER 40 OF 91 CAPLUS

Rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride; 2004:496322 CAPLUS

L5 ANSWER 41 OF 91 CAPLUS

Rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent: comparison with nateglinide; 2004:345396 CAPLUS

L5 ANSWER 42 OF 91 CAPLUS

Characterization of hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel hypoglycemic agent: comparison with glibenclamide, a sulfonylurea; 2004:345395 CAPLUS

L5 ANSWER 43 OF 91 CAPLUS

Preparation of arylhydroxypyrazoles for treatment of metabolic disorders; 2004:333698 CAPLUS

L5 ANSWER 44 OF 91 CAPLUS

Cardiovascular risk in type 2 diabetics and pharmacological regulation of mealtime glucose excursions; 2004:202949 CAPLUS

L5 ANSWER 45 OF 91 CAPLUS

Bicyclic oligopeptides and their use as glucagon receptor antagonists; 2004:60541 CAPLUS

L5 ANSWER 46 OF 91 CAPLUS

Bicyclic oligopeptides and their use as glucagon receptor antagonists; 2004:60532 CAPLUS

L5 ANSWER 47 OF 91 CAPLUS

Drug composition for prevention or inhibition of advance of diabetic complication; 2004:20487 CAPLUS

L5 ANSWER 48 OF 91 CAPLUS

Drug composition for blood sugar control; 2004:20486 CAPLUS

L5 ANSWER 49 OF 91 CAPLUS

Antidiabetic preparation for oral administration; 2004:3671 CAPLUS

L5 ANSWER 50 OF 91 CAPLUS

Pharmacology of the meglitinide analogs: new treatment options for type 2 diabetes mellitus; 2003:1000347 CAPLUS

L5 ANSWER 51 OF 91 CAPLUS

Therapeutic agent for diabetes; 2003:931184 CAPLUS

L5 ANSWER 52 OF 91 CAPLUS

Uptake of tritiated mitiglinide by pancreatic pieces and islets; 2003:780556 CAPLUS

L5 ANSWER 53 OF 91 CAPLUS

Combination of a HMG-CoA reductase inhibitor and an insulin secretion enhancer; 2003:777602 CAPLUS

L5 ANSWER 54 OF 91 CAPLUS

Oral pharmaceutical composition containing mitiglinide; 2003:573217 CAPLUS

L5 ANSWER 55 OF 91 CAPLUS

Use of an immediate-release powder in pharmaceutical and nutraceutical compositions; 2003:511859 CAPLUS

L5 ANSWER 56 OF 91 CAPLUS

Pharmaceutical compositions containing a renin inhibitor and antidiabetics; 2003:473243 CAPLUS

L5 ANSWER 57 OF 91 CAPLUS

Synergistic antidiabetic combinations containing antihyperlipemics and hydroximic acids; 2003:76614 CAPLUS

L5 ANSWER 58 OF 91 CAPLUS

Effects of S 21403 on hormone secretion from isolated rat pancreas at different glucose concentrations; 2002:894053 CAPLUS

L5 ANSWER 59 OF 91 CAPLUS

Processes for preparation of optically active 2-benzylsuccinic acid and optically active 2-benzylsuccinic acid monoamides; 2002:832745 CAPLUS

L5 ANSWER 60 OF 91 CAPLUS

Study of the insulinotropic effect of the novel antihyperglycemic agent KAD-1229 using HIT T15 cells, a hamster's insulinoma cell line; 2002:743481 CAPLUS

L5 ANSWER 61 OF 91 CAPLUS

Compositions comprising a polypeptide and an active agent; 2002:556104 CAPLUS

L5 ANSWER 62 OF 91 CAPLUS

Effect of KAD-1229, a novel hypoglycaemic agent, on plasma glucose levels after meal load in type 2 diabetic rats; 2002:395747 CAPLUS

L5 ANSWER 63 OF 91 CAPLUS

Compositions comprising a polypeptide and an active agent; 2002:332011 CAPLUS

L5 ANSWER 64 OF 91 CAPLUS

Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester; 2002:293592 CAPLUS

L5 ANSWER 65 OF 91 CAPLUS

Pharmaceutical compositions containing AT-receptor antagonist or insulin secretion enhancers; 2002:157602 CAPLUS

L5 ANSWER 66 OF 91 CAPLUS

Combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors; 2002:157564 CAPLUS

L5 ANSWER 67 OF 91 CAPLUS

A combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for the treatment of diabetes; 2002:51257 CAPLUS

L5 ANSWER 68 OF 91 CAPLUS

Absence of exacerbation of myocardial stunning in anesthetized dogs treated with KAD-1229, a novel hypoglycemic agent; 2001:864540 CAPLUS

L5 ANSWER 69 OF 91 CAPLUS

The effects of mitiglinide (KAD-1229), a new antidiabetic drug, on ATP-sensitive K⁺ channels and insulin secretion: comparison with the sulfonylureas and nateglinide; 2001:857058 CAPLUS

L5 ANSWER 70 OF 91 CAPLUS

Antidiabetic agents containing α-glucosidase inhibitors and insulin secretion promoters; 2001:635931 CAPLUS

L5 ANSWER 71 OF 91 CAPLUS

Rapid acting insulinotropic agents: restoration of early insulin secretion as a physiologic approach to improve glucose control; 2001:620286 CAPLUS

L5 ANSWER 72 OF 91 CAPLUS

Effects of mitiglinide (s 21403) on Kir6.2/SUR1, Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive potassium channel; 2001:282226 CAPLUS

L5 ANSWER 73 OF 91 CAPLUS

Effect of KAD-1229, a nonsulfonylurea hypoglycemic agent, on plasma glucose and insulin in streptozotocin-induced diabetic dogs; 2001:166771 CAPLUS

L5 ANSWER 74 OF 91 CAPLUS

Immediate-release oral pharmaceutical compositions containing benzylsuccinate derivatives; 2000:841976 CAPLUS

L5 ANSWER 75 OF 91 CAPLUS

Use of succinic acid derivatives to obtain a medicine for treating inflammation; 2000:814308 CAPLUS

L5 ANSWER 76 OF 91 CAPLUS

Recent developments and emerging therapies for type 2 diabetes mellitus; 2000:194936 CAPLUS

L5 ANSWER 77 OF 91 CAPLUS

Antidiabetic oral formulations containing benzylsuccinic acid derivative; 2000:59962 CAPLUS

L5 ANSWER 78 OF 91 CAPLUS

Effect of the Meglitinide analog S21403 on cationic fluxes and insulin release in perfused rat pancreatic islets exposed to a high concentration od D- Glucose; 1999:573477 CAPLUS

L5 ANSWER 79 OF 91 CAPLUS

Process for producing benzylsuccinic acid derivatives; 1998:527315 CAPLUS

L5 ANSWER 80 OF 91 CAPLUS

Process for producing optically active benzylsuccinic acid by optical resolution; 1998:527305 CAPLUS

L5 ANSWER 81 OF 91 CAPLUS

Effect of a novel hypoglycemic agent, KAD-1229 on glucose metabolism and fructose-2, 6- bisphosphate content in isolated hepatocytes of normal rats; 1996:730982 CAPLUS

L5 ANSWER 82 OF 91 CAPLUS

Effect of the meglitinide analog KAD-1229 on 45Ca outflow and insulin release in

pancreatic islets; 1996:647356 CAPLUS

L5 ANSWER 83 OF 91 CAPLUS

Effects of the methyl esters of pyruvate, succinate and glutamate on the secretory response to meglitinide analogs in rat pancreatic islets; 1996:584776 CAPLUS

L5 ANSWER 84 OF 91 CAPLUS

A rapid- and short-acting hypoglycemic agent KAD-1229 improves post-prandial hyperglycemia and diabetic complications in streptozotocin-induced non-insulin-dependent diabetes mellitus rats; 1996:536607 CAPLUS

L5 ANSWER 85 OF 91 CAPLUS

Effect of a non-sulfonylurea hypoglycemic agent, KAD-1229 on hormone secretion in the isolated perfused pancreas of the rat; 1996:269911 CAPLUS

L5 ANSWER 86 OF 91 CAPLUS

Insulinotropic action of meglitinide analogs: modulation by an activator of ATP-sensitive K⁺ channels and high extracellular K⁺ concentrations; 1996:156362 CAPLUS

L5 ANSWER 87 OF 91 CAPLUS

Insulinotropic action of (2S)-2-benzyl-3-(cis- hexahydro-2-isoindolinylcarbonyl) propionate I. Secretory and cationic aspects; 1995:747679 CAPLUS

L5 ANSWER 88 OF 91 CAPLUS

Normalization of impaired glucose tolerance by the short-acting hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2- isoindolinylcarbonyl)propionate dihydrate (KAD-1229) in non-insulin-dependent diabetes mellitus rats; 1995:477544 CAPLUS

L5 ANSWER 89 OF 91 CAPLUS

Inhibition of ATP-sensitive K⁺ channel by a non-sulfonylurea compound KAD-1229 in a pancreatic β-cell line, MIN 6 cell; 1995:231935 CAPLUS

L5 ANSWER 90 OF 91 CAPLUS

Novel rapid- and short-acting hypoglycemic agent, a calcium(2s)- 2-benzyl-3-(cis-hexahydro-2- isoindolinylcarbonyl)propionate (KAD-1229) that acts on the sulfonylurea receptor: comparison of effects between KAD-1229 and gliclazide; 1994:426648 CAPLUS

L5 ANSWER 91 OF 91 CAPLUS

Preparation of succinic acid azabicyclamides and related compounds as antidiabetics; 1993:59584 CAPLUS

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Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD :

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * * * * Welcome to STN International * * * * * * * * * * * * *

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NEWS 30 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields

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NEWS 32 MAY 21 TOXCENTER enhanced with BIOSIS reload
NEWS 33 MAY 21 CA/CAplus enhanced with additional kind codes for German patents
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=> file caplus
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.21 | 0.21 |

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=> e mitiglinide
E1 1 MITIGEAGE/BI
E2 1 MITIGEN/BI
E3 90 --> MITIGLINIDE/BI
E4 1 MITIGLNIDE/BI
E5 4 MITIGRATION/BI
E6 1 MITIGATION/BI
E7 2 MITII/BI
E8 1 MITIKAS/BI
E9 1 MITIKO/BI
E10 1 MITIKOGANE/BI
E11 1 MITILAN/BI
E12 3 MITILANE/BI

=> S e3-4
90 MITIGLINIDE/BI
1 MITIGLNIDE/BI
L1 90 (MITIGLINIDE/BI OR MITIGLNIDE/BI)

=> s reg
1347 REG
82 REGS
L2 1416 REG
(REG OR REGS)

=> d l2 1-5 ibib

L2 ANSWER 1 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

L2 ANSWER 2 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

L2 ANSWER 3 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

L2 ANSWER 4 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

L2 ANSWER 5 OF 1416 CAPLUS COPYRIGHT 2007 ACS on STN

=> his
HIS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (>).

=> d his

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E MITIGLINIDE

L1 90 S E3-4
L2 1416 S REG

=> s l1 AND diabet
=> d l1 IBIB

L1 ANSWER 1 OF 90 CAPLUS COPYRIGHT 2007 ACS on STN

=> file registry
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
16.87 17.08

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=> e mitiglinide

| | | |
|-----|----|--------------------|
| E1 | 1 | MITIGAL/BI |
| E2 | 1 | MITIGAN/BI |
| E3 | 2 | --> MITIGLINIDE/BI |
| E4 | 1 | MITIL/BI |
| E5 | 14 | MITILYSIN/BI |
| E6 | 10 | MITIN/BI |
| E7 | 1 | MITINDO/BI |
| E8 | 1 | MITINDOMIDE/BI |
| E9 | 4 | MITINE/BI |
| E10 | 2 | MITION/BI |
| E11 | 3 | MITIPH/BI |
| E12 | 3 | MITIPHYL/BI |

=> s e2-e4

| | | |
|----|---|--|
| | 1 | MITIGAN/BI |
| | 2 | MITIGLINIDE/BI |
| | 1 | MITIL/BI |
| L3 | 4 | (MITIGAN/BI OR MITIGLINIDE/BI OR MITIL/BI) |

=> d

L3 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

=> d l3 1-4

L3 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

L3 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

L3 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

L3 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

=> file caplus

COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 27.30 | 44.38 |

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=> s 145525-41-3 OR mitiglinide

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L5 53 L4

L6 90 MITIGLINIDE
 128 L5 OR MITIGLINIDE

=> s 16 and (diabetes OR diabetic OR diabetic complication OR postprandial hypoglycemia OR glycemic control or glucose)

125073 DIABETES
65399 DIABETIC
9086 DIABETICS
69423 DIABETIC
 (DIABETIC OR DIABETICS)
65399 DIABETIC
9086 DIABETICS
69423 DIABETIC
 (DIABETIC OR DIABETICS)
12197 COMPLICATION
35072 COMPLICATIONS
44255 COMPLICATION
 (COMPLICATION OR COMPLICATIONS)
2688 DIABETIC COMPLICATION
 (DIABETIC (W) COMPLICATION)
7857 POSTPRANDIAL
1 POSTPRANDIALS
7857 POSTPRANDIAL
 (POSTPRANDIAL OR POSTPRANDIALS)
13989 HYPOGLYCEMIA
48 HYPOGLYCEMIAS
14010 HYPOGLYCEMIA
 (HYPOGLYCEMIA OR HYPOGLYCEMIAS)
37 POSTPRANDIAL HYPOGLYCEMIA
 (POSTPRANDIAL (W) HYPOGLYCEMIA)
6108 GLYCEMIC
1587652 CONTROL
336796 CONTROLS

1806258 CONTROL
(CONTROL OR CONTROLS)
3436 GLYCEMIC CONTROL
(GLYCEMIC (W) CONTROL)
423129 GLUCOSE
823 GLUCOSSES
423309 GLUCOSE
(GLUCOSE OR GLUCOSSES)

L7 85 L6 AND (DIABETES OR DIABETIC OR DIABETIC COMPLICATION OR POSTPRANDIAL HYPOGLYCEMIA OR GLYCEMIC CONTROL OR GLUCOSE)

=> d 1-5 ibib

L7 ANSWER 1 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

L7 ANSWER 2 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

L7 ANSWER 3 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

L7 ANSWER 4 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

L7 ANSWER 5 OF 85 CAPLUS COPYRIGHT 2007 ACS on STN

=> FIL STNGUIDE
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
29.89 75.19

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=>

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=>
Executing the logoff script...

=> LOG Y

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FULL ESTIMATED COST ENTRY SESSION
0.06 75.25

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PASSWORD :

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| NEWS | 14 | FEB 26 | EMBASE enhanced with Clinical Trial Number field |
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=> d his

(FILE 'HOME' ENTERED AT 17:50:50 ON 22 MAY 2007)

=> file caplus

COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL
ENTRY SESSION
0.21 0.21

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=> S 145525-41-3

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=> s 12 and mitiglinide
90 MITIGLINIDE

L3 15 L2 AND MITIGLINIDE

=> s 13 and (diabetic or diabetes or diabetic complication or postprandial or glycemic or glucose)

65399 DIABETIC

9086 DIABETICS

69423 DIABETIC

(DIABETIC OR DIABETICS)

125073 DIABETES

65399 DIABETIC

9086 DIABETICS

69423 DIABETIC

(DIABETIC OR DIABETICS)

12197 COMPLICATION

35072 COMPLICATIONS

44255 COMPLICATION

(COMPLICATION OR COMPLICATIONS)

2688 DIABETIC COMPLICATION

(DIABETIC(W) COMPLICATION)

7857 POSTPRANDIAL

1 POSTPRANDIALS

7857 POSTPRANDIAL

(POSTPRANDIAL OR POSTPRANDIALS)

6108 GLYCEMIC

423129 GLUCOSE

823 GLUCOSSES

423309 GLUCOSE

(GLUCOSE OR GLUCOSSES)

L4 6 L3 AND (DIABETIC OR DIABETES OR DIABETIC COMPLICATION OR POSTPRANDIAL OR GLYCEMIC OR GLUCOSE)

=> d 1-6

.L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

.L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

=> FIL STNGUIDE

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY

SESSION

26.11

27.24

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```
=> save
ENTER L#, L# RANGE, ALL, OR (END):all
ENTER NAME OR (END):10519102
10519102 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,
structure, or screen set), /A for an answer
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):finn10519102
FINN10519102 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,
structure, or screen set), /A for an answer
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):finn519102
FINN519102 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,
structure, or screen set), /A for an answer
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):finn519102/a
'FINN519102/A' IS NOT ALLOWED WITH ALL
The saved name of an L# list must end with '/L'.
```

```
=> SAVE L1,L2,L3,L4 FINN10519102/L
L# LIST L1,L2,L3,L4 HAS BEEN SAVED AS 'FINN10519102/L'
```

```
=> log off
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
STN INTERNATIONAL LOGOFF AT 17:55:43 ON 22 MAY 2007
```

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * * * * Welcome to STN International * * * * * * * * * * *

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:30:38 ON 30 MAY 2007

| | | |
|--|---------------------|------------------|
| => file registry
COST IN U.S. DOLLARS | SINCE FILE
ENTRY | TOTAL
SESSION |
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 14:31:12 ON 30 MAY 2007

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 29 MAY 2007 HIGHEST RN 936074-26-9
DICTIONARY FILE UPDATES: 29 MAY 2007 HIGHEST RN 936074-26-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stndoc/properties.html>

=> s mitiglinide
L1 2 MITIGLINIDE

=> d 11

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN

=> s 11
L2 2 MITIGLINIDE

=> file caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| | |
|---------------------|------------------|
| SINCE FILE
ENTRY | TOTAL
SESSION |
| 13.20 | 13.41 |

FILE 'CAPLUS' ENTERED AT 14:33:11 ON 30 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 30 May 2007 VOL 146 ISS 23
FILE LAST UPDATED: 29 May 2007 (20070529/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s 11
L3 129 L1

=> d 13 1-10 IBIB

.L3 ANSWER 1 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 2 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 3 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 4 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 5 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 6 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 7 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 8 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 9 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

.L3 ANSWER 10 OF 129 CAPLUS COPYRIGHT 2007 ACS on STN

=> d his

(FILE 'HOME' ENTERED AT 14:30:38 ON 30 MAY 2007)

FILE 'REGISTRY' ENTERED AT 14:31:12 ON 30 MAY 2007
L1 2 S MITIGLINIDE
L2 2 S L1

FILE 'CAPLUS' ENTERED AT 14:33:11 ON 30 MAY 2007
L3 129 S L1

=> e mitiglinide
E1 1 MITIGEAGE/BI
E2 1 MITIGEN/BI
E3 91 --> MITIGLINIDE/BI
E4 1 MITIGLNIDE/BI

| | | |
|-----|---|---------------|
| E5 | 4 | MITIGATION/BI |
| E6 | 1 | MITIGATION/BI |
| E7 | 2 | MITII/BI |
| E8 | 1 | MITIKAS/BI |
| E9 | 1 | MITIKO/BI |
| E10 | 1 | MITIKOGANE/BI |
| E11 | 1 | MITILAN/BI |
| E12 | 3 | MITILANE/BI |

=> s L3 or mitiglinide
91 MITIGLINIDE
L4 139 L3 OR MITIGLINIDE

=> s 4 and (diabetes or diabet or postprandial or diabetic or glycemic or complication or (glucose level))
OR IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (>).

=> s 14 and (diabetes or diabet or postprandial or diabetic or glycemic or complication or (glucose level))
OR IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (>).

=> s 14 and (diabetic or diabetes or postprandial or glycemic or complication or glucose)
65527 DIABETIC
9096 DIABETICS
69552 DIABETIC
(DIABETIC OR DIABETICS)
125400 DIABETES
7888 POSTPRANDIAL
1 POSTPRANDIALS
7888 POSTPRANDIAL
(POSTPRANDIAL OR POSTPRANDIALS)
6137 GLYCEMIC
12238 COMPLICATION
35176 COMPLICATIONS
44391 COMPLICATION
(COMPLICATION OR COMPLICATIONS)
423650 GLUCOSE
823 GLUCOSSES
423830 GLUCOSE
(GLUCOSE OR GLUCOSSES)
L5 91 L4 AND (DIABETIC OR DIABETES OR POSTPRANDIAL OR GLYCEMIC OR COMPLICATION OR GLUCOSE)

=> save
ENTER L#, L# RANGE, ALL, OR (END):all
ENTER NAME OR (END):10519155
10519155 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:

1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
5. Not already be in use as a saved name,

- 6. Not be END, SAV, SAVE, SAVED
 - 7. Not have the form of an L-number (Lnnn).
- ENTER NAME OR (END):finn053007
FINN053007 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query, answer set, or L-number list. The name must:
 - 1. Begin with a letter,
 - 2. Have 1-12 characters,
 - 3. Contain only letters (A-Z) and numbers (0-9),
 - 4. End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
 - 5. Not already be in use as a saved name,
 - 6. Not be END, SAV, SAVE, SAVED
 - 7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn5307
FINN5307 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query, answer set, or L-number list. The name must:

- 1. Begin with a letter,
- 2. Have 1-12 characters,
- 3. Contain only letters (A-Z) and numbers (0-9),
- 4. End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
- 5. Not already be in use as a saved name,
- 6. Not be END, SAV, SAVE, SAVED
- 7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn530
FINN530 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query, answer set, or L-number list. The name must:

- 1. Begin with a letter,
- 2. Have 1-12 characters,
- 3. Contain only letters (A-Z) and numbers (0-9),
- 4. End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
- 5. Not already be in use as a saved name,
- 6. Not be END, SAV, SAVE, SAVED
- 7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn5
FINN5 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query, answer set, or L-number list. The name must:

- 1. Begin with a letter,
- 2. Have 1-12 characters,
- 3. Contain only letters (A-Z) and numbers (0-9),
- 4. End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
- 5. Not already be in use as a saved name,
- 6. Not be END, SAV, SAVE, SAVED
- 7. Not have the form of an L-number (Lnnn).

ENTER NAME OR (END):finn053007/a
'FINN053007/A' IS NOT ALLOWED WITH ALL
The saved name of an L# list must end with '/L'.

=> finn053007/1
FINN053007 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

| | | |
|----------------------|------------|---------|
| => FIL STNGUIDE | SINCE FILE | TOTAL |
| COST IN U.S. DOLLARS | ENTRY | SESSION |
| FULL ESTIMATED COST | 31.98 | 45.39 |

FILE 'STNGUIDE' ENTERED AT 14:40:55 ON 30 MAY 2007
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 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: May 25, 2007 (20070525/UP).

=> SAVE L1,L2,L3,L4,L5 FINN053007/L
 L# LIST L1,L2,L3,L4,L5 HAS BEEN SAVED AS 'FINN053007/L'

| | | |
|----------------------|------------|---------|
| => log hold | SINCE FILE | TOTAL |
| COST IN U.S. DOLLARS | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.06 | 45.45 |

SESSION WILL BE HELD FOR 120 MINUTES
 STN INTERNATIONAL SESSION SUSPENDED AT 14:41:35 ON 30 MAY 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
 SESSION RESUMED IN FILE 'STNGUIDE' AT 14:46:39 ON 30 MAY 2007
 FILE 'STNGUIDE' ENTERED AT 14:46:39 ON 30 MAY 2007
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 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

| | | |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| FULL ESTIMATED COST | ENTRY | SESSION |
| | 0.06 | 45.45 |

=> dis his

(FILE 'HOME' ENTERED AT 14:30:38 ON 30 MAY 2007)

FILE 'REGISTRY' ENTERED AT 14:31:12 ON 30 MAY 2007
 L1 2 S MITIGLINIDE
 L2 2 S L1

FILE 'CAPLUS' ENTERED AT 14:33:11 ON 30 MAY 2007
 L3 129 S L1
 E MITIGLINIDE
 L4 139 S L3 OR MITIGLINIDE
 L5 91 S L4 AND (DIABETIC OR DIABETES OR POSTPRANDIAL OR GLYCEMIC OR C

FILE 'STNGUIDE' ENTERED AT 14:40:55 ON 30 MAY 2007
 SAVE L1,L2,L3,L4,L5 FINN053007/L

=> s 15 and diabetes
 0 MITIGLINIDE

0 MITIGLINIDE
0 DIABETIC
1 DIABETES
0 POSTPRANDIAL
0 GLYCEMIC
0 COMPLICATION
0 GLUCOSE
1 DIABETES
L6 0 L5 AND DIABETES

=> d 15 1-91 ibib
YOU HAVE REQUESTED DATA FROM FILE 'CAPLUS' - CONTINUE? (Y)/N:y

L5 ANSWER 1 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 2 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 3 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 4 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 5 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 6 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 7 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 8 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 9 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 10 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 11 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 12 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 13 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 14 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 15 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 16 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 17 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 18 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 19 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 20 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 21 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 22 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 23 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 24 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 25 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 26 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

.L5 ANSWER 27 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

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.L5 ANSWER 41 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

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L5 ANSWER 85 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 86 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 87 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 88 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 89 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 90 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

L5 ANSWER 91 OF 91 CAPLUS COPYRIGHT 2007 ACS on STN

=> log hold

COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE
ENTRY | TOTAL
SESSION |
|---------------------|------------------|
| 0.06 | 153.54 |

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:48:59 ON 30 MAY 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamrf1614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * *

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 JAN 08 CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 3 JAN 16 CA/CAplus Company Name Thesaurus enhanced and reloaded

NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN
NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6 JAN 22 CA/CAPLUS updated with revised CAS roles
NEWS 7 JAN 22 CA/CAPLUS enhanced with patent applications from India
NEWS 8 JAN 29 PHAR reloaded with new search and display fields
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10 FEB 15 PATD/PASPC enhanced with Drug Approval numbers
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13 FEB 26 MEDLINE reloaded with enhancements
NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field
NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE
NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19 MAR 16 CASREACT coverage extended
NEWS 20 MAR 20 MARPAT now updated daily
NEWS 21 MAR 22 LWPI reloaded
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN
NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records
NEWS 26 APR 30 CA/CAPLUS enhanced with 1870-1889 U.S. patent records
NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN
NEWS 28 MAY 01 New CAS web site launched
NEWS 29 MAY 08 CA/CAPLUS Indian patent publication number format defined
NEWS 30 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 31 MAY 21 BIOSIS reloaded and enhanced with archival data
NEWS 32 MAY 21 TOXCENTER enhanced with BIOSIS reload
NEWS 33 MAY 21 CA/CAPLUS enhanced with additional kind codes for German patents
NEWS 34 MAY 22 CA/CAPLUS enhanced with IPC reclassification in Japanese patents

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 17:53:06 ON 06 JUN 2007

=> activate

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of

commands which can be used in this file.

=> activate saved

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> d his

(FILE 'HOME' ENTERED AT 17:53:06 ON 06 JUN 2007)

=> saved

SAVED IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> activate 102/A

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> log off

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:y

STN INTERNATIONAL LOGOFF AT 17:54:19 ON 06 JUN 2007

10/519155

***** QUERY RESULTS *****

=> d his 133

(FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007)
L33 24 S L32 OR L24

=> d que 133

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 145375-43-5/RN
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON 207844-01-7/RN
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON MITIGLINIDE/CN
L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L4 OR L5 OR L6)
L9 97 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR MITIGLINIDE CALCIUM
 HYDRATE/OBI
L10 87 SEA FILE=HCAPLUS ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI(W)
 GLINIDE/OBI
L11 108 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 OR L10
L13 2160940 SEA FILE=HCAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI
 OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
 PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)
L19 110617 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABET?/OBI
L20 54 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L19
L22 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 (5A) L20
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY
 <2004 OR REVIEW/DT
L24 17 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L23
L27 271 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A)
 (POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI)
L28 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L27
L29 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI
L30 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 OR L29
L31 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND L30
L32 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 OR L31
L33 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 OR L24

=> d his 149

(FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007)
L49 33 S L48 (P) L13

=> d que 149

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 145375-43-5/RN
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON 207844-01-7/RN
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON MITIGLINIDE/CN
L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L4 OR L5 OR L6)
L10 87 SEA FILE=HCAPLUS ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI(W)
 GLINIDE/OBI
L13 2160940 SEA FILE=HCAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI
 OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
 PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)
L19 110617 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABET?/OBI
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY
 <2004 OR REVIEW/DT
L27 271 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A)
 (POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI)
L29 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI
L43 84 SEA L8
L44 172 SEA L10

L45 10 SEA MITIGLINIDE CALCIUM HYDRATE
 L46 173 SEA (L43 OR L44 OR L45)
 L47 110 SEA L46 AND (L19 OR L27 OR L29)
 L48 46 SEA L47 AND L23
 L49 33 SEA L48 (P) L13

=> dup rem l33 l49
 FILE 'HCAPLUS' ENTERED AT 15:07:58 ON 24 MAY 2007
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 PROCESSING COMPLETED FOR L33
 PROCESSING COMPLETED FOR L49
 L61 49 DUP REM L33 L49 (8 DUPLICATES REMOVED)
 ANSWERS '1-24' FROM FILE HCAPLUS
 ANSWERS '25-42' FROM FILE MEDLINE
 ANSWERS '43-45' FROM FILE EMBASE
 ANSWERS '46-49' FROM FILE DRUGU

=> d 161 1-24 ibib ed abs hitind

L61 ANSWER 1 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:505268 HCAPLUS Full-text
 DOCUMENT NUMBER: 145:483552
 TITLE: Therapeutic efficacy of mitiglinide combined
 with once daily insulin glargine after switching from
 multiple daily insulin regimen of aspart insulin and
 glargine in patients with type 2 diabetes mellitus
 AUTHOR(S) : Yoshihara, Tomoaki; Kumashiro, Naoki; Kanazawa,
 Yoshie; Mita, Tomoya; Sakurai, Yuko; Kawai, Junko;
 Abe, Michiko; Motojima, Kayoko; Hara, Kanako;
 Yamazaki, Yuka; Kanazawa, Akio; Miwa, Shinya; Sato,
 Fumihiro; Kanno, Rei; Shimizu, Tomoaki; Sakai, Ken;
 Uchino, Hiroshi; Watada, Hirotaka; Tanaka, Yasushi;
 Kawamori, Ryuzo; Hirose, Takahisa
 CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology,
 School of Medicine, Juntendo University, Bunkyo-ku,
 Tokyo, 113-8421, Japan
 SOURCE: Endocrine Journal (Kyoto, Japan) (2006), 53(1), 67-72
 CODEN: ENJOEO; ISSN: 0918-8959
 PUBLISHER: Japan Endocrine Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 31 May 2006
 AB Mitiglinide is novel class of rapid-acting insulin secretagogues, which have
 been widely used alone or in combination with other oral hypoglycemic drugs to
 improve postprandial hyperglycemia in early type 2 diabetes. While mitiglinide
 enhances postprandial requirement of insulin, the efficacy of mitiglinide

combined with insulin has yet to be established. We investigated the efficacy of metformin combined with insulin glargine, the first soluble insulin analog that has a flat and prolonged effect. After control with the intensive regimen (daily aspart insulin and glargine), 30 inpatients with type 2 diabetes were switched to premeal metformin combined with once daily insulin glargine (metformin regimen), and daily profiles of blood glucose level were compared under each regimen. Fifteen patients showed similar control of hyperglycemia with metformin regimen and intensive insulin regimen, assessed by M value (<32), while the remaining 15 showed worsening under the metformin regimen. The patients who were well controlled with metformin regimen were significantly younger (51.9 ± 16.0 years, $p<0.005$) and heavier (body mass index: 25.7 ± 3.3 kg/m 2 , $p<0.05$) than those who were not (67.9 ± 8.7 and 23.0 ± 3.1 , resp.). Moreover, insulin doses of aspart per body weight were significantly fewer in effective group than in ineffective group. Duration of diabetes was shorter in the effective group, albeit insignificantly. Previous treatment before starting intensive insulin regimen, such as insulin and sulfonylurea, was not different between the two groups. Our results suggest that metformin plus insulin glargine combination therapy is useful for lowering both fasting and postprandial hyperglycemia in a subpopulation of type 2 diabetes. The long-term effects of such treatment need to be established in future studies.

- CC 1-10 (Pharmacology)
 ST metformin insulin glargine hyperglycemia type2
 diabetes mellitus antidiabetic
 IT Antidiabetic agents
 Body weight
 Combination chemotherapy
 Human
 Hyperglycemia
 (metformin combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)
 IT Glycerides, biological studies
 High-density lipoproteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (metformin combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)
 IT Diabetes mellitus
 (non-insulin-dependent; metformin combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)
 IT 50-99-7, D-Glucose, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (blood; metformin combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)
 IT 57-88-5, Cholesterol, biological studies 62572-11-6, Hemoglobin A1c
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (metformin combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)
 IT 9004-10-8, Insulin, biological studies 145375-43-5,
 Metformin 160337-95-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and postprandial hyperglycemia in patient with type 2 diabetes mellitus)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:962511 HCAPLUS Full-text

DOCUMENT NUMBER: 143:244659

TITLE: Method for examining blood glucose control state

INVENTOR(S): Kitahara, Yoshiro; Miura, Kyoko; Takeuchi, Masayoshi

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2005080993 | A1 | 20050901 | WO 2005-JP3438 | 20050223 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | JP 2004-47020 | A 20040223 |

ED Entered STN: 02 Sep 2005

AB A novel diagnostic marker for a blood glucose control state is provided. Also provided is a method for diagnosing or examining a blood glucose control state. The method comprises a process for measuring the AGE2 concentration in a blood or body fluid sample of a patient by a measuring method selected from a Western blotting method, an enzyme immunoassay, a RIA, a liquid chromatog. and a dot blot method, and a process for evaluating the state of postprandial hyperglycemia control.

IC ICM G01N033-68

ICS G01N033-15; G01N033-50; G01N033-53; G01N033-577; G01N033-66

CC 9-10 (Biochemical Methods)

Section cross-reference(s): 14

IT Hyperglycemia

(postprandial; method for examining blood glucose control state by measuring blood AGE2)

IT 54870-28-9D, Meglitinide, derivative 105816-04-4, Nateglinide 135062-02-1, Repaglinide 145375-43-5, Mitiglinide

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method for examining blood glucose control state by measuring blood AGE2)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

10/519155

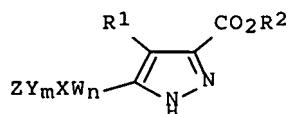
ACCESSION NUMBER: 2005:120729 HCAPLUS Full-text
 DOCUMENT NUMBER: 142:219276
 TITLE: Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases
 INVENTOR(S): Semple, Graeme; Gharbaoui, Tawfik; Shin, Young-Jun; Decaire, Marc; Averbuj, Claudia; Skinner, Philip J.
 PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 130 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------------|
| WO 2005011677 | A1 | 20050210 | WO 2004-US18389 | 20040610 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG | | | | |
| AU 2004260636 | A1 | 20050210 | AU 2004-260636 | 20040610 <-- |
| CA 2528834 | A1 | 20050210 | CA 2004-2528834 | 20040610 <-- |
| EP 1633351 | A1 | 20060315 | EP 2004-776418 | 20040610 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| US 2007032537 | A1 | 20070208 | US 2006-560332 | 20060908 <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-478664P | P 20030613 <-- |
| | | | WO 2004-US18389 | W 20040610 |

OTHER SOURCE(S): MARPAT 142:219276

ED Entered STN: 11 Feb 2005

GI



AB Title compds. [I; W, Y = (substituted) alkylene, alkenylene, alkynylene; X = NR₃CO, NR₃SO₂, NR₃, CO, CH(OH), C(NH), O, S, SO, SO₂, etc.; R₃, R₄ = H, (substituted) alkyl, Ph, heteroaryl; Z = H, halo, (substituted) Ph, heteroaryl; R₁ = H, OH, halo, alkyl, haloalkyl; R₂ = H, alkyl; m, n = 0, 1; with provisos], were prepared. Thus, 5-methylthiomethyl-2H-pyrazole-3-carboxylic acid (preparation outlined) showed hRUP25 agonist activity with EC₅₀ = 4.3 μM.

IC ICM A61K031-415
 ICS C07D231-14; A61P003-06
 CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63
 ST pyrazolecarboxylate prepn RUP25 nicotinic acid receptor agonist;
 dyslipidemia atherosclerosis heart disease diabetes obesity
 treatment pyrazolecarboxylate prepn
 IT Diabetes mellitus
 (non-insulin-dependent, treatment; preparation of pyrazolecarboxylates as
 agonists for the RUP25 nicotinic acid receptor for the treatment of
 dyslipidemia and related diseases)
 IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin
 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide
 535-65-9, Glybutethiazole 631-27-6, Glyclopypamide 637-07-0, Clofibrate
 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin
 882-09-7, Clofibrate acid 968-81-0, Acetohexamide 1156-19-0, Tolazamide
 1228-19-9, Glypinamide 1492-02-0, Glybzole 3149-00-6, Phenbutamide
 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8,
 Glibenclamide 14929-11-4, Simfibrate 21187-98-4, Gliclazide
 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9,
 Glibornuride 29094-61-9, Glipizide 30299-08-2, Clinofibrate
 31637-97-5, Etofibrate 31980-29-7, Nicofibrate 33342-05-1, Gliquidone
 41859-67-0, Bezafibrate 42597-57-9, Ronifibrate, biological studies
 49562-28-9, Fenofibrate 52214-84-3, Ciprofibrate 54504-70-0,
 Theofibrate 55285-45-5, Pirifibrate 55937-99-0, Beclobrate
 56180-94-0, Acarbose 62571-86-2, Captopril 68367-52-2, Sorbinil
 69047-39-8, Binifibrate 72432-03-2, Miglitol 74258-86-9, Alacepril
 75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat
 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin
 82159-09-9, Epalrestat 82834-16-0, Perindopril 82964-04-3, Tolrestat
 83435-66-9, Delapril 83480-29-9, Voglibose 83647-97-6, Spirapril
 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril
 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril
 89371-37-9, Imidapril 89391-50-4, Imirestat 93479-97-1, Glimepiride
 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4,
 Nateglinide 110703-94-1, Zopolrestat 111025-46-8, Pioglitazone
 111223-26-8, Ceronapril 111902-57-9, Temocapril 112733-06-9,
 Zenarestat 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin
 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin
 287714-41-4, Rosuvastatin
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (coadministration; preparation of pyrazolecarboxylates as agonists for the
 RUP25 nicotinic acid receptor for the treatment of dyslipidemia and
 related diseases)
 IT 9001-42-7, α -Glucosidase 9028-31-3, Aldose reductase
 9028-35-7, Hmg coa reductase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors coadministration; preparation of pyrazolecarboxylates
 as agonists for the RUP25 nicotinic acid receptor for the treatment of
 dyslipidemia and related diseases)
 IT 9015-82-1
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors, coadministration; preparation of pyrazolecarboxylates
 as agonists for the RUP25 nicotinic acid receptor for the treatment of
 dyslipidemia and related diseases)
 IT 111-02-4, Squalene
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (synthesis inhibitors coadministration; preparation of
 pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor
 for the treatment of dyslipidemia and related diseases)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 4 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:1009580 HCPLUS Full-text
 DOCUMENT NUMBER: 144:142642
 TITLE: Effects of S21403 (mitiglinide) on postprandial generation of oxidative stress and inflammation in type 2 diabetic patients
 AUTHOR(S): Assaloni, R.; Ros, R. Da; Quagliaro, L.; Piconi, L.; Maier, A.; Zuodar, G.; Motz, E.; Ceriello, A.
 CORPORATE SOURCE: Department of Pathology and Medicine, Experimental and Clinical, University of Udine, Udine, Italy
 SOURCE: Diabetologia (2005), 48(9), 1919-1924
 CODEN: DBTGAJ; ISSN: 0012-186X
 PUBLISHER: Springer GmbH
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 19 Sep 2005
 AB Aim/hypothesis: Evidence suggests that postprandial hyperglycemia may be a cardiovascular risk factor in diabetes. Oxidative stress and inflammation are involved in the pathogenesis of diabetic complications and previous studies have shown increased oxidative stress and inflammation in the postprandial phase in diabetic patients. The aim of the present study was to evaluate whether controlling postprandial hyperglycemia with S21403 (mitiglinide) is accompanied by a reduced generation of oxidative stress and inflammation. Subjects and methods: Forty type 2 diabetic patients participated in the study. Two different breakfast-tests were performed in each patient, with placebo or S21403. Plasma nitrotyrosine, plasma malondialdehyde (MDA), oxidized LDL (oxLDL), plasma total radical-trapping antioxidant parameter (TRAP), IL-6, IL-18, TNF- α , plasma glucose and insulin were measured. Results: After the administration of S21403, 40 mg, a rapid stimulation of insulin secretion was observed, accompanied by a reduction of postprandial hyperglycemia. With S21403, a significant decrease of either nitrotyrosine, MDA and oxLDL levels, and a preservation of plasma TRAP compared with placebo was found. Significant decreases of IL-6, IL-18 and TNF- α were also observed with S21403 compared with placebo. Conclusions/interpretation: This study shows that controlling postprandial hyperglycemia with S21403 significantly improves the cluster of oxidative stress and inflammation markers that are increased in the postprandial state in diabetic patients.
 CC 1-10 (Pharmacology)
 ST mitiglinide postprandial hyperglycemia
 oxidative stress inflammation diabetes antidiabetic
 IT Receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (SSR (signal sequence receptor); controlling postprandial hyperglycemia with S21403 significantly decreased oxidative stress markers nitrotyrosine, MDA, oxLDL levels and preserved plasma TRAP in type 2 diabetic patient)
 IT Interleukin 18
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (controlling postprandial hyperglycemia with S21403 significantly decreased inflammatory marker interleukin-18 in type 2 diabetic patient)
 IT Interleukin 6
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (controlling postprandial hyperglycemia with S21403 significantly decreased inflammatory marker interleukin-6 in type 2 diabetic patient)
 IT Tumor necrosis factors

- RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (controlling postprandial hyperglycemia with S21403
 significantly decreased inflammatory marker tumor necrosis
 factor- α in type 2 diabetic patient)
- IT Inflammation
 (controlling postprandial hyperglycemia with S21403
 significantly decreased inflammatory markers IL-6, IL-18, TNF- α
 in type 2 diabetic patient)
- IT Human
Hyperglycemia
Pancreas
 (controlling postprandial hyperglycemia with S21403
 significantly decreased oxidative stress markers nitrotyrosine, MDA,
 oxLDL levels, inflammatory markers IL-6, IL-18, TNF- α and
 preserved plasma TRAP in type 2 diabetic patient)
- IT Oxidative stress, biological
 (controlling postprandial hyperglycemia with S21403
 significantly decreased oxidative stress markers nitrotyrosine,
 malondialdehyde, oxLDL levels and preserved plasma TRAP in type 2
 diabetic patient)
- IT Antidiabetic agents
 (controlling postprandial hyperglycemia with
 mitiglinide significantly decreased oxidative stress markers
 nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18,
 TNF- α and preserved plasma TRAP in type 2 diabetic patient)
- IT Diabetes mellitus
 (non-insulin-dependent; controlling postprandial
 hyperglycemia with S21403 significantly decreased oxidative
 stress markers nitrotyrosine, MDA, oxLDL levels, inflammatory markers
 IL-6, IL-18, TNF- α and preserved plasma TRAP in type 2 diabetic
 patient)
- IT Low-density lipoproteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (oxidized; controlling postprandial hyperglycemia
 with S21403 significantly decreased oxidative stress marker oxLDL
 levels in type 2 diabetic patient)
- IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological
 studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (S21403 stimulated insulin secretion which was accompanied by reduction of
 postprandial hyperglycemia in type 2 diabetic
 patient)
- IT 542-78-9, Malondialdehyde
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (controlling postprandial hyperglycemia with S21403
 significantly decreased oxidative stress marker malondialdehyde in type
 2 diabetic patient)
- IT 621-44-3
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (controlling postprandial hyperglycemia with S21403
 significantly decreased oxidative stress marker nitrotyrosine in type 2
 diabetic patient)
- IT 145375-43-5, Mitiglinide
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (controlling postprandial hyperglycemia with
 mitiglinide significantly decreased oxidative stress markers
 nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18,
 TNF- α and preserved plasma TRAP in type 2 diabetic patient)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 5 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:902180 HCPLUS Full-text
 DOCUMENT NUMBER: 141:355415
 TITLE: A synergistic pharmaceutical combination comprising cicletanine for the prevention or treatment of diabetes
 INVENTOR(S): Egri, Janos
 PATENT ASSIGNEE(S): Synosens Kutato es Fejleszto Kft., Hung.
 SOURCE: PCT Int. Appl., 29 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------------|
| WO 2004091612 | A1 | 20041028 | WO 2004-HU37 | 20040414 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG | | | | |
| HU 200300990 | A2 | 20050530 | HU 2003-990 | 20030415 <-- |
| CA 2522126 | A1 | 20041028 | CA 2004-2522126 | 20040414 <-- |
| EP 1648453 | A1 | 20060426 | EP 2004-727331 | 20040414 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| JP 2006523668 | T | 20061019 | JP 2006-506248 | 20040414 <-- |
| PRIORITY APPLN. INFO.: | | | HU 2003-990 | A 20030415 <-- |
| | | | WO 2004-HU37 | W 20040414 |

OTHER SOURCE(S): MARPAT 141:355415

ED Entered STN: 28 Oct 2004

AB The invention refers to a synergistic pharmaceutical combination comprising (a) a first pharmaceutical composition containing cicletanine or a pharmaceutically suitable acid addition salt thereof and one or more conventional carrier(s), and (b) a second pharmaceutical composition containing an antidiabetic or antihyperlipidemic active agent or, if desired and chemical possible, a pharmaceutically suitable acid addition salt or a salt formed with a pharmaceutically suitable base thereof and one or more conventional carrier(s). An antidiabetic agent is selected from a thiazolidinedione derivative, a sulfonylurea, or a biguanidine derivative. The pharmaceutical combination is suitable for the prevention or treatment of a prediabetic state, metabolic X-syndrome or diabetes mellitus, as well as disorders associated with these states.

IC ICM A61K031-4355
 ICS A61K031-155; A61K031-427; A61K031-64; A61P003-00; A61P003-10

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 2

ST cicletanine antidiabetic hypolipemic synergy diabetes complication

- IT Hair, disease
 (diffuse effluvium; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Metabolic disorders
 (metabolic syndrome X; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Antidiabetic agents
 (oral; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Ovary, disease
 (polycystic; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Alopecia
 Antidiabetic agents
 Combination chemotherapy
 Diabetes mellitus
 Hypolipemic agents
 (synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Dyslipidemia
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Sulfonylureas
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT Drug interactions
 (synergistic; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT 10238-21-8, Glyburide
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Glibenclamide; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT 9004-10-8, Insulin, biological studies
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (resistance; synergistic combination comprising cicletanine for prevention or treatment of diabetes and related disorders)
- IT 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 631-27-6, Glyclopypamide 637-07-0, Clofibrate 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1492-02-0, Glybzole 2295-31-0D, Thiazolidinedione, derivs. 5868-05-3, Niceritrol 6882-47-9D, Biguanidine, derivs. 10571-59-2, Nicoclionate 11041-12-6, Cholestyramine 14929-11-4, Simfibrate 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 27959-26-8, Nicomol 29094-61-9, Glipizide 31637-97-5, Etofibrate 32797-92-5, Glisentide 33342-05-1, Gliquidone 42597-57-9, Ronifibrate, biological studies 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 56180-94-0, Acarbose 56227-39-5, Polidexide 72432-03-2, Miglitol 74772-77-3, Ciglitazone 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82747-56-6, Cicletanine hydrochloride

10/519155

83480-29-9, Voglibose 89943-82-8, Cicletanine 93479-97-1, Glimepiride
93957-54-1, Fluvastatin 97322-87-7, Troglitazone 105816-04-4,
Senaglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone
134523-00-5, Atorvastatin 135062-02-1, Repaglinide 145375-43-5
. Mitiglinide

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic combination comprising cicletanine for prevention
or treatment of diabetes and related disorders)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

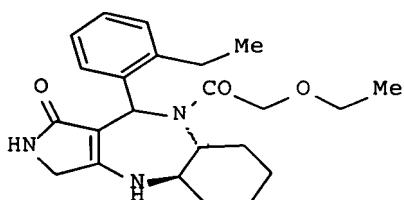
L61 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:681582 HCAPLUS Full-text
DOCUMENT NUMBER: 141:185111
TITLE: Remedy for **diabetes**
INVENTOR(S): Ikenoue, Takao; Kageyama, Yoko; Iino, Yukio; Kondo, Nobuo
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|----------------|
| WO 2004069259 | A1 | 20040819 | WO 2004-JP1279 | 20040206 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004210268 | A1 | 20040819 | AU 2004-210268 | 20040206 <-- |
| CA 2515294 | A1 | 20040819 | CA 2004-2515294 | 20040206 <-- |
| EP 1595544 | A1 | 20051116 | EP 2004-708897 | 20040206 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2004007303 | A | 20060207 | BR 2004-7303 | 20040206 <-- |
| CN 1771040 | A | 20060510 | CN 2004-80009410 | 20040206 <-- |
| US 2005272641 | A1 | 20051208 | US 2005-198511 | 20050808 <-- |
| PRIORITY APPLN. INFO.: | | | JP 2003-31088 | A 20030207 <-- |
| | | | WO 2004-JP1279 | A 20040206 |

OTHER SOURCE(S) : MARPAT 141:185111

ED Entered STN: 20 Aug 2004

GI



AB A preventive and/or a remedy for diabetes, diabetic complications, hyperinsulinemia, sugar metabolic error or obesity characterized by comprising a combination of a compound represented by the following formula (I; Markush's structures given), its analog or a pharmaceutically acceptable salt thereof with a hypoglycemic agent.

IC ICM A61K031-5517
 ICS A61K031-551; A61K031-553; A61K031-554; A61P003-04; A61P003-10;
 A61P043-00; A61K045-00; C07D487-04

CC 1-10 (Pharmacology)
 Section cross-reference(s) : 2

IT Nerve, disease
 (diabetic neuropathy; heterocyclic compds. as antidiabetic and antiobesity agents)

IT Antidiabetic agents
 Antihypertensives
 Antiobesity agents
 Antioxidants
 Diabetes mellitus
 Drug resistance
 Obesity
 β3-Adrenoceptor agonists
 (heterocyclic compds. as antidiabetic and antiobesity agents)

IT 56-03-1D, Biguanide, derivs. 114-86-3, Fenformin 657-24-9, Metformin 692-13-7, Buformin 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 56180-94-0, Acarbose 105816-04-4, Nateglinide 111025-46-8,
 Pioglitazone 122320-73-4, Rosiglitazone 145375-43-5,
 Mitiglinide 433729-78-3 433729-79-4 433729-80-7
 433729-81-8 433729-82-9 433729-83-0 433729-84-1 433729-85-2
 433729-86-3 433729-87-4 433729-88-5 433729-89-6 433729-90-9
 433729-91-0 433729-92-1 433729-93-2 433729-94-3 433729-95-4
 433729-96-5 433729-97-6 433729-98-7 433729-99-8 433730-00-8
 433730-01-9 433730-02-0 433730-03-1 433730-04-2 433730-05-3
 433730-06-4 433730-07-5 433730-08-6 433730-09-7 433730-10-0
 433730-11-1 433730-12-2 433730-13-3 433730-14-4 433730-15-5
 433730-16-6 433730-17-7 433730-18-8 433730-19-9 433730-20-2
 433730-21-3 433730-22-4 433730-23-5 433730-24-6 433730-25-7
 433730-26-8 433730-27-9 433730-28-0 433730-29-1 433730-30-4
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 433730-36-0 433730-37-1 433730-38-2 433730-39-3 433730-40-6
 433730-41-7 433730-42-8 433730-43-9 433730-44-0 433730-45-1
 433730-46-2 433730-47-3 433730-48-4 433730-49-5 433730-50-8
 433730-51-9 433730-52-0 433730-53-1 433730-54-2 433730-55-3
 433730-56-4 433730-57-5 433730-58-6 433730-59-7 433730-60-0
 433730-61-1 433730-62-2 433730-63-3 433730-64-4 433730-65-5
 433730-66-6 433730-67-7 433730-68-8 433730-69-9 433730-70-2
 433730-72-4 433730-73-5 433730-75-7 433730-76-8 433730-77-9
 433730-78-0 433730-79-1 433730-80-4 433730-81-5 433730-82-6
 433730-83-7 433730-84-8 433730-85-9 433730-86-0 433730-87-1
 433730-88-2 433730-89-3 433730-90-6 433730-91-7 433730-92-8
 433730-93-9 433730-94-0 433730-95-1 433730-96-2 433730-97-3
 433730-98-4 433730-99-5 433731-00-1 433731-01-2 433731-02-3
 433731-04-5 433731-06-7 433731-08-9 433731-09-0 433731-10-3
 433731-11-4 737804-07-8 737804-08-9 737804-09-0 737804-10-3
 737804-11-4 737804-12-5 737804-13-6 737804-14-7 737804-15-8
 737804-16-9 737804-17-0 737804-18-1 737804-19-2 737804-20-5
 737804-21-6 737804-22-7 737804-23-8 737804-24-9 737804-25-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (heterocyclic compds. as antidiabetic and antiobesity agents)
 IT 9001-62-1, Lipase 9028-31-3, Aldose reductase 9035-74-9,
 Glycogen phosphorylase 54249-88-6, Dipeptidyl peptidase IV
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; heterocyclic compds. as antidiabetic and
 antiobesity agents)

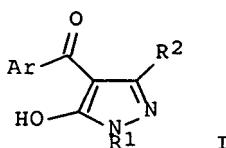
L61 ANSWER 7 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:333698 HCPLUS Full-text
 DOCUMENT NUMBER: 140:357333
 TITLE: Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders
 INVENTOR(S): Semple, Graeme; Shin, Young Jun
 PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 125 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|---|----------------|
| WO 2004033431 | A2 | 20040422 | WO 2003-US31509 | 20031002 <-- |
| WO 2004033431 | A3 | 20040729 | | |
| | | | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | |
| AU 2003282679 | A1 | 20040504 | AU 2003-282679 | 20031002 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-416193P | P 20021004 <-- |
| | | | US 2002-417120P | P 20021007 <-- |
| | | | WO 2003-US31509 | W 20031002 <-- |

OTHER SOURCE(S): MARPAT 140:357333

ED Entered STN: 23 Apr 2004

GI



AB Title compds. [I; R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, benzyl, optionally substituted with ≥1 halo, OH, cyano, NO₂, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl,

alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl, arylureyl; R2 = H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, PhCH₂, Ph, heteroaryl, optionally substituted with ≥1 halo, OH, cyano, nitro, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfmyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl or arylureyl groups; Ar = (substituted) pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl], were prepared for the treatment of metabolic-related disorders, including dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, type 2 diabetes, Syndrome-X and the like (no data). Thus, nicotinyl chloride, 2-methyl-5-propyl-2,4-dihydropyrazol-3-one, and Ca(OH)₂ were heated at 90° in dioxane for 2 h. to give (5-hydroxy-1-methyl-3-propyl-1H-pyrazol-4-yl)pyridin-3-ylmethanone. It may be used in combination with other active agents such α-glucosidase inhibitors, aldose reductase inhibitors, biguanides, HMG-CoA reductase inhibitors, squalene synthesis inhibitors, fibrates, LDL catabolism enhancers, angiotensin converting enzyme inhibitors, and insulin secretion enhancers.

| | |
|----|---|
| IC | ICM C07D231-00 |
| CC | 28-8 (Heterocyclic Compounds (More Than One Hetero Atom)) |
| | Section cross-reference(s): 1 |
| IT | Diabetes mellitus
(non-insulin-dependent; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders) |
| IT | 56-03-1, Biguanide 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopymamide 637-07-0, Clofibrate 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin 882-09-7, Clofibrate acid 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybzole 2295-31-0D, Thiazolidinedione, derivs 3149-00-6, Phenbutamide 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 14929-11-4, Simfibrate 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 29094-61-9, Glipizide 30299-08-2, Clinofibrate 31637-97-5, Etofibrate 31980-29-7, Nicofibrate 33342-05-1, Gliquidone 41859-67-0, Bezafibrate 42597-57-9, Ronifibrate, biological studies 49562-28-9, Fenofibrate 52214-84-3, Ciprofibrate 54504-70-0, Theofibrate 55285-45-5, Pirifibrate 55937-99-0, Beclobrate 56180-94-0, Acarbose 62571-86-2, Captopril 68367-52-2, Sorbinil 69047-39-8, Binifibrate 74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82159-09-9, Epalrestat 82834-16-0, Perindopril 82964-04-3, Tolrestat 83435-66-9, Delapril 83480-29-9, Voglibose 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 89391-50-4, Imirestat 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4, Nateglinide 110703-94-1, Zopolrestat 111025-46-8, Pioglitazone 111223-26-8, Ceronapril 111902-57-9, Temocapril 112733-06-9, Zenarestat 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders) |
| IT | 9001-42-7, α-Glucosidase 9015-82-1, Angiotensin converting enzyme |

9028-31-3, Aldose reductase 9028-35-7, HMG-CoA
 reductase 9077-14-9, Squalene synthase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors coadministration; preparation of aroylhydroxypyrazoles
 for treatment of metabolic disorders)

L61 ANSWER 8 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:60541 HCPLUS Full-text
 DOCUMENT NUMBER: 140:105298
 TITLE: Bicyclic oligopeptides and their use as glucagon
 receptor antagonists
 INVENTOR(S): Potterat, Olivier; Streicher, Ruediger; Wagner, Klaus;
 Maurer, Till; Mack, Juergen; Peters, Stefan
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
 SOURCE: PCT Int. Appl., 33 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------------|
| WO 2004007535 | A1 | 20040122 | WO 2003-EP7657 | 20030715 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2489189 | A1 | 20040122 | CA 2003-2489189 | 20030715 <-- |
| AU 2003246702 | A1 | 20040202 | AU 2003-246702 | 20030715 <-- |
| EP 1525218 | A1 | 20050427 | EP 2003-763864 | 20030715 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006505507 | T | 20060216 | JP 2004-520641 | 20030715 <-- |
| US 2004072736 | A1 | 20040415 | US 2003-621272 | 20030717 <-- |
| US 7101848 | B2 | 20060905 | | |
| PRIORITY APPLN. INFO.: | | | EP 2002-15907 | A 20020717 <-- |
| | | | US 2002-416797P | P 20021008 <-- |
| | | | WO 2003-EP7657 | W 20030715 <-- |

OTHER SOURCE(S): MARPAT 140:105298

ED Entered STN: 26 Jan 2004

AB The invention relates to a bicyclic oligopeptide or ester thereof having the capability to inhibit the glucagon receptor, which essentially consists of (a) a first cyclic group, which comprises at least one cysteine group and is formed by an amide bonding of the N-terminal amino acid with the second carboxylate group of a diacid amino acid, and (b) a second cyclic group which is formed by an amide bonding of an amino acid with the -carboxylate group of said diacid amino acid, and by a disulfide bonding of the C-terminal cysteine and a cysteine group within the first cyclic group (a); and to the use of such bicyclic oligopeptides for the preparation of a medicament for the treatment or prevention of diseases, in which glucagon receptors are involved.

IC ICM C07K007-56
 ICS A61K038-12; C07K014-36

CC 1-10 (Pharmacology)

Section cross-reference(s): 2, 10, 34, 63

ST bicyclic oligopeptide glucagon receptor inhibition disease treatment; diabetes treatment bicyclic oligopeptide glucagon receptor inhibition

IT Proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (ALBP (adipocyte lipid-binding protein), inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Streptomyces
 (DSM 14996, bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Transport proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (SGLT2 (sodium-dependent glucose transporter 2), inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon-like peptide-1 receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
 (ampoules; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Actinomycetes
 (bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Antidiabetic agents
 Antiobesity agents
 Cardiovascular agents
 Diabetes mellitus
 Human
 Peroxisome proliferators
 (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
 (capsules; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
 (carriers; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Peptides, biological studies
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclic; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and

- metabolic stability)
- IT Lipids, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (modulating agents; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT Retinoid X receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (modulators; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT Drug delivery systems
 (suppositories; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT Drug delivery systems
 (tablets, coated; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT Drug delivery systems
 (tablets; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α , modulators; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (γ , modulators; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT 145375-43-5, Mitiglinide
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (analogs; bicyclic oligopeptides as glucagon receptor
 inhibitors in relation to disease treatment and combination
 with other agents and metabolic stability)
- IT 9007-92-5, Glucagon, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (bicyclic oligopeptides as glucagon receptor inhibitors in
 relation to disease treatment and combination with other agents and
 metabolic stability)
- IT 647807-35-0P
 RL: BSU (Biological study, unclassified); NPO (Natural product
 occurrence); PAC (Pharmacological activity); PUR (Purification or
 recovery); THU (Therapeutic use); BIOL (Biological study); OCCU
 (Occurrence); PREP (Preparation); USES (Uses)
 (bicyclic oligopeptides as glucagon receptor inhibitors in
 relation to disease treatment and combination with other agents and
 metabolic stability)
- IT 647807-36-1P
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (bicyclic oligopeptides as glucagon receptor inhibitors in
 relation to disease treatment and combination with other agents and
 metabolic stability)
- IT 9004-10-8, Insulin, biological studies

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT 56-03-1D, Biguanide, derivs. 94-20-2, Chloropropamide 657-24-9, Metformin 10238-21-8, Glyburide 21187-98-4, Gliclazide 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 97322-87-7, Troglitazone 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 141732-76-5, Exendin-4 161600-01-7, Isaglitazone
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT 9033-06-1, Glucosidase 54249-88-6, Dipeptidyl peptidase IV 300865-11-6, Protein tyrosine phosphatase 1B 391208-93-8, Glycogen synthase kinase 3
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:60532 HCAPLUS Full-text
 DOCUMENT NUMBER: 140:105297
 TITLE: Bicyclic oligopeptides and their use as glucagon receptor antagonists
 INVENTOR(S): Potterat, Olivier; Streicher, Ruediger; Wagner, Klaus; Maurer, Till; Mack, Juergen; Peters, Stefan
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|----------------|
| WO 2004007524 | A2 | 20040122 | WO 2003-EP7311 | 20030708 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2003260306 | A1 | 20040202 | AU 2003-260306 | 20030708 <-- |
| US 2004072736 | A1 | 20040415 | US 2003-621272 | 20030717 <-- |
| US 7101848 | B2 | 20060905 | | |
| PRIORITY APPLN. INFO.: | | | EP 2002-15907 | A 20020717 <-- |
| | | | US 2002-416797P | P 20021008 <-- |

OTHER SOURCE(S) : MARPAT 140:105297

ED Entered STN: 26 Jan 2004

AB The invention relates to a bicyclic oligopeptide or ester thereof having the capability to inhibit the glucagon receptor, which essentially consists of (a) a first cyclic group, which comprises at least one cysteine group and is formed by an amide bonding of the N-terminal amino acid with the second carboxylate group of a diacid amino acid, and (b) a second cyclic group which is formed by an amide bonding of an amino acid with the -carboxylate group of said diacid amino acid, and by a disulfide bonding of the C-terminal cysteine and a cysteine group within the first cyclic group (a); and to the use of such bicyclic oligopeptides for the preparation of a medicament for the treatment or prevention of diseases, in which glucagon receptors are involved.

IC ICM C07K

CC 1-10 (Pharmacology)

Section cross-reference(s) : 10, 34, 63

ST bicyclic oligopeptide glucagon receptor inhibition disease treatment; diabetes treatment bicyclic oligopeptide glucagon receptor inhibition

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (ALBP (adipocyte lipid-binding protein), inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Streptomyces

(DSM 14996, bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Transport proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (SGLT2 (sodium-dependent glucose transporter 2), inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon-like peptide-1 receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems

(ampoules; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Actinomycetes

(bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Antidiabetic agents

Antiobesity agents

Cardiovascular agents

Diabetes mellitus

Human

(bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and

- metabolic stability)
- IT Drug delivery systems
 - (capsules; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems
 - (carriers; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Peptides, biological studies
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (cyclic; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Lipids, biological studies
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (modulating agents; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Retinoid X receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (modulators; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems
 - (suppositories; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems
 - (tablets, coated; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Drug delivery systems
 - (tablets; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (α , agonists; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT Peroxisome proliferator-activated receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (γ , modulators; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT 145375-43-5, Mitiglinide
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (analogs; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT 9007-92-5, Glucagon, biological studies
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT 647807-35-0P
 - RL: BSU (Biological study, unclassified); NPO (Natural product)

- occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
- (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT 647807-36-1P
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT 9004-10-8, Insulin, biological studies
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT 56-03-1D, Biguanide, derivs. 94-20-2, Chloropropamide 657-24-9, Metformin 10238-21-8, Glyburide 21187-98-4, Gliclazide 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 97322-87-7, Troglitazone 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 141732-76-5, Exendin-4 161600-01-7, Isaglitazone
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)
- IT 9033-06-1, Glucosidase 54249-88-6, Dipeptidyl peptidase IV 300865-11-6, Protein tyrosine phosphatase 1B 391208-93-8, Glycogen synthase kinase 3
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; bicyclic oligopeptides as glucagon receptor inhibitors in relation to disease treatment and combination with other agents and metabolic stability)

L61 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:20487 HCAPLUS Full-text
 DOCUMENT NUMBER: 140:65256
 TITLE: Drug composition for prevention or inhibition of advance of diabetic complication
 INVENTOR(S): Mikoshiba, Imao; Suzuki, Hisao; Kiyono, Yuji
 PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 22 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|-------------|
| WO 2004002474 | A1 | 20040108 | WO 2003-JP8084 | 20030626 <- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, | | | | |

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
 PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
 TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2489660 A1 20040108 CA 2003-2489660 20030626 <--
 AU 2003244083 A1 20040119 AU 2003-244083 20030626 <--
 EP 1552830 A1 20050713 EP 2003-761816 20030626 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1665499 A 20050907 CN 2003-815245 20030626 <--
 US 2005215607 A1 20050929 US 2004-519155 20041227 <--
 PRIORITY APPLN. INFO.: JP 2002-189559 A 20020628 <--
 WO 2003-JP8084 W 20030626 <--

ED Entered STN: 11 Jan 2004

AB Disclosed is a drug composition capable of attaining a good state of blood sugar control so as to enable correcting postprandial high blood sugar levels or high blood sugar levels at early fasting time. In particular, a drug composition for prevention or inhibition of advance of diabetic complications to be taken before meals, comprising 5 to 45 mg, in terms of one-time dose, of mitiglinide or its pharmacol. acceptable salt or a hydrate thereof, e.g., mitiglinide calcium salt hydrate. The drug composition is highly useful for the prevention or inhibition of advance of, for example, diabetic microangio complications and arteriosclerosis because the ratio of occurrence of side effects, such as low blood sugar level symptom and gastrointestinal tract disorder, is low. A tablet containing mitiglinide calcium salt hydrate 10 mg/tablet was formulated, and its effect on blood sugar level and side effect in patients with type 2 diabetes was examined

IC ICM A61K031-4035
 ICS A61P003-10; A61P009-00; A61P009-10; A61P013-12; A61P027-02;
 A61P043-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST mitiglinide diabetic complication treatment oral

IT Blood vessel, disease

(diabetic microangiopathy; drug composition for prevention or inhibition of advance of diabetic complication)

IT Kidney, disease

(diabetic nephropathy; drug composition for prevention or inhibition of advance of diabetic complication)

IT Eye, disease

(diabetic retinopathy; drug composition for prevention or inhibition of advance of diabetic complication)

IT Arteriosclerosis

(diabetic; drug composition for prevention or inhibition of advance of diabetic complication)

IT Human

(drug composition for prevention or inhibition of advance of diabetic complication)

IT Diabetes mellitus

(non-insulin-dependent; drug composition for prevention or inhibition of advance of diabetic complication)

IT Antidiabetic agents

(oral; drug composition for prevention or inhibition of advance of diabetic complication)

IT Drug delivery systems

(tablets; drug composition for prevention or inhibition of advance of diabetic complication)

IT 50-99-7, D-Glucose, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (blood; drug composition for prevention or inhibition of
 advance of diabetic complication)

IT 145375-43-5, Mitiglinide 207844-01-7
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (drug composition for prevention or inhibition of
 advance of diabetic complication)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:20486 HCAPLUS Full-text

DOCUMENT NUMBER: 140:65255

TITLE: Drug composition for blood sugar control

INVENTOR(S): Mikoshiba, Imao; Suzuki, Hisao; Kiyono, Yuji

PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2004002473 | A1 | 20040108 | WO 2003-JP8083 | 20030626 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2490250 | A1 | 20040108 | CA 2003-2490250 | 20030626 |
| AU 2003244082 | A1 | 20040119 | AU 2003-244082 | 20030626 |
| EP 1532979 | A1 | 20050525 | EP 2003-761815 | 20030626 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1665498 | A | 20050907 | CN 2003-815244 | 20030626 |
| US 2005267195 | A1 | 20051201 | US 2004-519102 | 20041227 |
| PRIORITY APPLN. INFO.: | | | JP 2002-189556 | A 20020628 |
| | | | WO 2003-JP8083 | W 20030626 |

ED Entered STN: 11 Jan 2004

AB Disclosed is a drug composition capable of attaining a good state of blood sugar control so as to enable correcting postprandial high blood sugar levels or high blood sugar levels at early fasting time. In particular, a drug composition for blood sugar control to be taken before meals, comprising 5 to 45 mg, in terms of one-time dose, of mitiglinide or its pharmacol. acceptable salt or a hydrate thereof, e.g., mitiglinide calcium salt hydrate. The drug composition is highly useful for the prevention and treatment of, for example, type 2 diabetes because the ratio of occurrence of side effects, such as low blood sugar level symptom and gastrointestinal tract disorder, is low. A tablet containing mitiglinide calcium salt hydrate 10 mg/tablet was formulated, and its effect on blood sugar level and side effect in patients with type 2 diabetes was examined

IC ICM A61K031-4035
 ICS A61P003-10; A61P043-00
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1
 ST mitiglinide oral type 2 antidiabetic
 IT Human
 Hyperglycemia
 (drug composition for blood sugar control containing mitiglinide)
 IT Diabetes mellitus
 (non-insulin-dependent; drug composition for blood sugar control containing mitiglinide)
 IT Antidiabetic agents
 (oral; drug composition for blood sugar control containing mitiglinide)
 IT Drug delivery systems
 (tablets; drug composition for blood sugar control containing mitiglinide)
 IT 50-99-7, D-Glucose, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (blood; drug composition for blood sugar control containing mitiglinide)
 IT 145375-43-5, Mitiglinide 207844-01-7
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (drug composition for blood sugar control containing mitiglinide)
 REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 12 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:496322 HCPLUS Full-text
 DOCUMENT NUMBER: 141:167555
 TITLE: Rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent.
 comparison with glimepiride
 AUTHOR(S): Ojima, Kazuma; Aoyagi, Ikumi; Fujimori, Yoshikazu;
 Ichikawa, Kiyoshi; Kusama, Hiroshi; Kojima, Masami;
 Nagasawa, Tatsuya; Ohta, Masanao; Okuhara, Yuji;
 Kobayashi, Maiko; Tamura, Kei; Kuroda, Junji; Shibata,
 Nobuo
 CORPORATE SOURCE: Pharmacology Research Lab. R&D, Kissei Pharmaceutical
 Co., Ltd., Japan
 SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(3),
 161-167
 CODEN: JPTABU
 PUBLISHER: Raifu Saiensu Shuppan K.K.
 DOCUMENT TYPE: Journal
 LANGUAGE: Japanese
 ED Entered STN: 21 Jun 2004
 AB The purpose of the present study was to evaluate the hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent, by comparing it with that of glimepiride, a sulfonylurea agent. In fasted beagle dogs, KAD-1229 (0.15, 0.3 mg/kg) or glimepiride (0.03, 0.06 mg/kg) was administered orally either with no load or just before an oral glucose load. Blood samples were taken from the cephalic vein for the determination of plasma glucose levels. In expts. with no load, plasma insulin levels were also measured. With no glucose load, the hypoglycemic effect of KAD-1229 had a faster onset (at 0.25 h) than that of glimepiride (at 1 h), and a shorter duration (0.25-1 h) than that of glimepiride (1-8 h). KAD-1229 stimulated insulin secretion, the peak level occurring within 0.25 h

and a return to baseline within 1 h. In contrast, the peak insulin level occurred at 1 h post-dose in the glimepiride groups. In the oral glucose tolerance test, KAD-1229 rapidly inhibited the increase in plasma glucose (at 0.25 h), and its effect had disappeared within 2 h after its administration. Glimepiride induced a lowering of the plasma glucose level at 1 h after its administration, and at a dose of 0.06 mg/kg, the glucose level given did not return to control values within 8 h. The hypoglycemic effect of KAD-1229 was clearly faster in onset and shorter lasting than that of glimepiride. KAD-1229 can be expected to be more effective than glimepiride at normalizing postprandial hyperglycemia.

- CC 1-10 (Pharmacology)
 IT Antidiabetic agents
 Diabetes mellitus
 (rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)
 IT 50-99-7, D-Glucose, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (blood; rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)
 IT 9004-10-8, Insulin, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)
 IT 93479-97-1, Glimepiride 145525-41-3, KAD-1229
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride)

L61 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2004:345396 HCAPLUS Full-text
 DOCUMENT NUMBER: 141:325483
 TITLE: Rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent: comparison with nateglinide
 AUTHOR(S): Ojima, Kazuma; Ichikawa, Kiyoshi; Fujimori, Yoshikazu;
 Aoyagi, Ikumi; Yamato, Tokuhisa; Tsuji, Atsutoshi;
 Kusama, Hiroshi; Kojima, Masami; Shibata, Nobuo
 CORPORATE SOURCE: Pharmacology Research R & D, Kissei Pharmaceutical Co., Ltd., Japan
 SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(2), 73-80
 CODEN: JPTABU
 PUBLISHER: Raifu Saiensu Shuppan K.K.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 28 Apr 2004
 AB Objectives: The purpose of the present study was to evaluate the insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent, by comparison with that of nateglinide. Methods: Mitiglinide calcium dihydrate or nateglinide was administered orally just before an oral-sucrose or liquid-meal load in normal rats, and in mild, moderate, or severe streptozotocin-injected diabetic rats. The plasma insulin and glucose levels were measured. Results: Mitiglinide calcium dihydrate (1 mg/kg) and nateglinide (50 mg/kg) decreased the plasma glucose levels

significantly at 15-120 min and 15-60 min, resp. in normal rats, and at 30-90 min and 30-60 min, resp., in mildly diabetic rats. These drugs increased the plasma insulin levels at 5-45 min and 5-15 min, resp., in normal rats, and at 15-60 min and 15-45 min, resp., in mildly diabetic rats. In moderately diabetic rats, the antihyperglycemic effects of mitiglinide calcium dihydrate (1 and 3 mg/kg) and nateglinide (50 and 100 mg/kg) were evident at 30-120 min and 30-60 min, resp. In the same rats, mitiglinide, but not nateglinide, significantly increased the plasma insulin levels at 30 min after its administration. Mitiglinide also exhibited antihyperglycemic and insulinotropic effects in the severely diabetic rats. Conclusion: Mitiglinide and nateglinide are suitable drugs for controlling postprandial hyperglycemia. Their antihyperglycemic effects were probably secondary to their rapid-onset, short-lasting insulinotropic effects, and mitiglinide seemed to be a more potent rapid-onset insulinotropic drug than nateglinide.

CC 1-10 (Pharmacology)

ST insulinotropic mitiglinide calcium dihydrate KAD1229
antipostpradial hyperglycemia nateglinide

IT Antidiabetic agents

Hyperglycemia

(rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostpradial hyperglycemic agent: comparison with nateglinide)

IT 105816-04-4, Nateglinide 145525-41-3, KAD-1229

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostpradial hyperglycemic agent: comparison with nateglinide)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:931184 HCAPLUS Full-text

DOCUMENT NUMBER: 140:8791

TITLE: Therapeutic agent for diabetes

INVENTOR(S): Nakanishi, Satoshi; Yano, Hiroshi; Mori, Kiyotoshi; Ogino, Fumiko; Kusaka, Hideaki; Ueno, Kimihisa; Nomoto, Yuji; Matsuda, Yuzuru

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2003097064 | A1 | 20031127 | WO 2003-JP6136 | 20030516 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003234929 | A1 | 20031202 | AU 2003-234929 | 20030516 <-- |

PRIORITY APPLN. INFO.:

JP 2002-143598

A 20020517 <--

WO 2003-JP6136

W 20030516 <--

OTHER SOURCE(S) : MARPAT 140:8791

ED Entered STN: 28 Nov 2003

AB A therapeutic agent for diabetes, is characterized by containing at least one member selected among sulfonylurea antidiabetic agents and sulfonylurea-free K₊ ATP channel blocker antidiabetic agents and at least one member selected among a fused purine derivative and pharmacol. acceptable salts of these. For example, a tablet contained glibenclamide 2, (R)-2-cyclopentyl-7,8-dihydro-8-(4-picoly)-4-propyl-1H-imidazo[2,1-i]-purin-5(4H)-one d-tartaric acid salt 18, lactose 143.4, starch 30, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg.

IC ICM A61K031-522

ICS A61K031-198; A61K031-4453; A61K031-64; A61K045-00; A61P003-10

CC 63-6 (Pharmaceuticals)

Section cross-reference(s) : 1

ST antidiabetic sulfonylurea potassium channel blocker purine deriv; tablet glibenclamide imidazopurine deriv antidiabetic combination

IT Potassium channel blockers

(ATP-sensitive; antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT Sulfonylureas

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT Drug delivery systems

(capsules; antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT Drug delivery systems

(tablets; antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 631-27-6, Glyclopypamide 664-95-9, Glycyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1492-02-0, Glybzol 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepide 26944-48-9, Glibornuride 29094-61-9, Glipizide 32797-92-5, Glisentide 33342-05-1, Gliquidone 93479-97-1, Glimepiride 105816-04-4, Nateglinide 135062-02-1, Repaglinide 145375-43-5, Mitiglinide 254426-47-6 348165-49-1 348362-73-2
349554-62-7 349554-69-4 627512-37-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic combinations for treatment and prevention of diabetes complications and side effects)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 15 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:777602 HCPLUS Full-text

DOCUMENT NUMBER: 139:296975

TITLE: Combination of a HMG-CoA reductase

inhibitor and an insulin secretion enhancer

INVENTOR(S) : Damon, Robert Edson; Hughes, Thomas Edward; Burkey, Bryan

PATENT ASSIGNEE(S) : Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-----------------|
| WO 2003080070 | A2 | 20031002 | WO 2003-EP2978 | 20030321 <-- |
| WO 2003080070 | A3 | 20040325 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU,
LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC,
SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR | | | | |
| CA 2479880 | A1 | 20031002 | CA 2003-2479880 | 20030321 <-- |
| AU 2003209745 | A1 | 20031008 | AU 2003-209745 | 20030321 <-- |
| US 2004002519 | A1 | 20040101 | US 2003-393798 | 20030321 <-- |
| EP 1523316 | A2 | 20050420 | EP 2003-744834 | 20030321 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1642559 | A | 20050720 | CN 2003-806655 | 20030321 <-- |
| JP 2005526788 | T | 20050908 | JP 2003-577896 | 20030321 <-- |
| BR 2003008613 | A | 20050301 | BR 2003-8613 | 20030324 <-- |
| NO 2004004487 | A | 20041220 | NO 2004-4487 | 20041020 <-- |
| US 2007027197 | A1 | 20070201 | US 2006-497130 | 20060801 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-366752P | P 20020322 <-- |
| | | | US 2003-393798 | B1 20030321 <-- |
| | | | WO 2003-EP2978 | W 20030321 <-- |

ED Entered STN: 03 Oct 2003

AB The present invention relates to a combination pharmaceutical composition comprising as active ingredients (i) a HMG-CoA reductase inhibitor or a salt, (ii) (a) an insulin secretion enhancer or a salt or (b) an insulin sensitizer or a salt. Thus, capsules contained fluvastatin sodium 42.962, CaCO₃ 125.680, NaHCO₃ 4.000, microcryst. cellulose 114.440, pregelatinized starch 83.800, Mg stearate 21.00, and talc 18.860 mg, and water qs.

IC ICM A61K031-64

ICS A61K031-40; A61K031-015; A61K031-435; A61K031-21; A61P005-50;
A61K031-404; A61K031-155; A61P003-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST insulin secretion enhancer HMGCoA reductase inhibitor

IT Drug delivery systems

(capsules; combination of HMG-CoA reductase inhibitor
and insulin secretion enhancer)

IT Antiarteriosclerotics

Antidiabetic agents

Antihypertensives

Antiobesity agents

Atherosclerosis

Hypertension

Hypolipemic agents

Hypothyroidism

Kidney, disease

Obesity

(combination of HMG-CoA reductase inhibitor and
insulin secretion enhancer)

- IT Dyslipidemia
 Hyperlipidemia
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (combination of HMG-CoA reductase inhibitor and
 insulin secretion enhancer)
- IT Sulfonylureas
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination of HMG-CoA reductase inhibitor and
 insulin secretion enhancer)
- IT Artery, disease
 (coronary; combination of HMG-CoA reductase inhibitor
 and insulin secretion enhancer)
- IT Kidney, disease
 (failure; combination of HMG-CoA reductase inhibitor
 and insulin secretion enhancer)
- IT Liver, disease
 (fatty; combination of HMG-CoA reductase inhibitor
 and insulin secretion enhancer)
- IT Heart, disease
 (infarction, survival post; combination of HMG-CoA reductase
 inhibitor and insulin secretion enhancer)
- IT Metabolic disorders
 (metabolic syndrome X; combination of HMG-CoA reductase
 inhibitor and insulin secretion enhancer)
- IT Diabetes mellitus
 (non-insulin-dependent; combination of HMG-CoA reductase
 inhibitor and insulin secretion enhancer)
- IT Ovary, disease
 (polycystic; combination of HMG-CoA reductase
 inhibitor and insulin secretion enhancer)
- IT Drug delivery systems
 (tablets; combination of HMG-CoA reductase inhibitor
 and insulin secretion enhancer)
- IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide
 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6 657-24-9,
 Metformin 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0,
 Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybzazole 3149-00-6,
 Phenbutamide 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea
 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1,
 Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide
 33342-05-1, Gliquidone 75330-75-5, Lovastatin 79902-63-9, Simvastatin
 81093-37-0, Pravastatin 89750-14-1, GLP-1 93479-97-1, Glimepiride
 93957-54-1, Fluvastatin 93957-55-2, Fluvastatin sodium 105816-04-4,
 Starlix DS 123475-27-4 134523-00-5, Atorvastatin 135062-02-1,
 Repaglinide 138347-77-0 145375-43-5, Mitiglinide
 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 207556-62-5
 223607-24-7 274901-16-5 287714-41-4, Rosuvastatin 352513-61-2
 355393-49-6 355393-50-9 355393-52-1
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination of HMG-CoA reductase inhibitor and
 insulin secretion enhancer)
- IT 9028-35-7, HMG-CoA reductase 54249-88-6, DPP-IV
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitor; combination of HMG-CoA reductase
 inhibitor and insulin secretion enhancer)
- IT 9004-10-8, Insulin, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (secretion enhancer; combination of HMG-CoA reductase
 inhibitor and insulin secretion enhancer)

L61 ANSWER 16 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2003:511859 HCPLUS Full-text
 DOCUMENT NUMBER: 139:90459
 TITLE: Use of an immediate-release powder in pharmaceutical
 and nutraceutical compositions
 INVENTOR(S): Besse, Jerome; Besse, Laurence
 PATENT ASSIGNEE(S): Fr.
 SOURCE: U.S. Pat. Appl. Publ., 5 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------------|
| US 2003124191 | A1 | 20030703 | US 2002-106923 | 20020325 <-- |
| FR 2834212 | A1 | 20030704 | FR 2001-16934 | 20011227 <-- |
| FR 2834212 | B1 | 20040709 | | |
| CA 2471903 | A1 | 20030710 | CA 2002-2471903 | 20021227 <-- |
| WO 2003055464 | A1 | 20030710 | WO 2002-FR4575 | 20021227 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002364489 | A1 | 20030715 | AU 2002-364489 | 20021227 <-- |
| EP 1458356 | A1 | 20040922 | EP 2002-799854 | 20021227 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002015380 | A | 20041207 | BR 2002-15380 | 20021227 <-- |
| US 2005118272 | A1 | 20050602 | US 2003-500213 | 20021227 <-- |
| JP 2005520799 | T | 20050714 | JP 2003-556042 | 20021227 <-- |
| HU 200500509 | A2 | 20050928 | HU 2005-509 | 20021227 <-- |
| NO 2004003172 | A | 20040914 | NO 2004-3172 | 20040726 <-- |
| PRIORITY APPLN. INFO.: | | | FR 2001-16934 | A 20011227 <-- |
| | | | WO 2002-FR4575 | W 20021227 <-- |

ED Entered STN: 04 Jul 2003

AB The present invention relates to the use of a powder comprising at least one active substance, at least one surfactant, at least one wetting agent and at least one diluent, for preparing a pharmaceutical or nutraceutical composition, this composition allowing rapid and immediate release of the active substance. Granules containing phloroglucinol 10, sorbitol 89, and propylene glycol 1% were prepared

IC ICM A61K031-7048

ICS A61K031-56; A61K031-522; A61K031-4965; A61K031-445; A61K031-573;
 A61K031-496; A61K031-4178; A61K031-135

INCL 424489000; 514182000; 514177000; 514178000; 514029000; 514649000;
 514317000; 514343000; 514263350; 514554000

CC 63-6 (Pharmaceuticals)

IT Diabetes mellitus

(non-insulin-dependent; use of immediate-release powder in pharmaceutical and nutraceutical compns.)

IT 39391-18-9, Cyclooxygenase

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors; use of immediate-release powder in pharmaceutical and nutraceutical compns.)

- IT 50-03-3, Hydrocortisone acetate 50-23-7, Hydrocortisone 50-28-2, Oestradiol, biological studies 50-28-2D, Oestradiol, derivs. 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 51-34-3, Scopolamine 51-98-9, Norethisterone acetate 54-11-5, Nicotine 54-21-7, Sodium salicylate 55-63-0, Trinitrin 56-81-5, Glycerol, biological studies 57-09-0, Cetrimonium bromide 57-13-6, Urea, biological studies 57-47-6, Physostigmine 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-55-6, Propylene glycol, biological studies 57-63-6, Ethinyl oestradiol 57-83-0, Progesterone, biological studies 58-08-2, Caffeine, biological studies 58-22-0, Testosterone 59-66-5, Acetazolamide 60-40-2, Mecamylamine 63-42-3, Lactose 64-17-5, Ethanol, biological studies 67-73-2, Fluocinolone acetonide 69-65-8, Mannitol 71-52-3, Bicarbonate, biological studies 81-13-0, Dexpanthenol 87-33-2, Isosorbide dinitrate 87-99-0, Xylitol 89-78-1, Menthol) 94-36-0, Benzoyl peroxide, biological studies 97-53-0, Eugenol 101-20-2, Triclocarban 106-24-1, Geraniol 106-25-2, Nerol 106-60-5, 5-Aminolevulinic acid 108-73-6, Phloroglucinol 110-27-0, Isopropyl myristate 112-62-9, Methyl oleate 112-80-1, Oleic acid, biological studies 113-45-1, Methyl phenidate 114-07-8, Erythromycin 123-03-5, Cetylpyridinium chloride 124-94-7, Triamcinolone 137-58-6, Lidocaine 139-33-3 143-07-7, Lauric acid, biological studies 144-80-9, Sulphacetamide 145-42-6, Sodium taurocholate 147-24-0, Diphenhydramine hydrochloride 151-21-3, Sodium lauryl sulphate, biological studies 152-97-6, Fluocortolone 302-79-4, Tretinoïn 303-40-2, Fluocortolone hexanoate 356-12-7, Fluocinolide 437-38-7, Fentanyl 443-48-1, Metronidazole 470-82-6, Eucalyptol 471-34-1, Calcium carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 521-18-6, Dihydrotestosterone 585-86-4, Lactitol 611-53-0, Ibacitabine 638-94-8, Desonide 645-92-1 745-65-3, Alprostadil 797-63-7, Levonorgestrel 863-57-0, Sodium glycocholate 1180-95-6, Sodium taurodeoxycholate 2002-29-1, Flumetasone pivalate 2152-44-5, Betamethasone valerate 2438-72-4, Bufexamac 3764-87-2 4205-90-7, Clonidine 4394-00-7, Nifluminic acid 4759-48-2, Isotretinoin 4985-25-5, Pyrazinobutazone 5104-49-4, Flurbiprofen 5593-20-4, Betamethasone dipropionate 5633-20-5, Oxybutynin 5716-20-1, Bamethan sulfate 6805-41-0, Escin 7757-93-9, Dibasic calcium phosphate 7758-87-4, Tribasic calcium phosphate 7759-35-5, Nestorone 7778-18-9, Calcium sulphate 9000-30-0, Guar gum 9002-72-6, Growth hormone 9003-39-8, Povidone 9004-10-8, Insulin, biological studies 9004-32-4, Sodium carboxymethylcellulose 9004-53-9, Dextrans 9004-57-3, Ethylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9004-67-5, Methylcellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-63-4D, Polyoxyethylene sorbitan, esters with fatty acids 9005-65-6, Polysorbate 80 9042-14-2, Dextran sulphate 9087-70-1, Aprotinin 12619-70-4, Cyclodextrins 12794-10-4, Benzodiazepine 14611-51-9, Selegiline 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16409-34-0, Sodium glycodeoxycholate 18559-94-9, Salbutamol 19216-56-9, Prazosin 22071-15-4, Ketoprofen 22832-87-7, Miconazole nitrate 22916-47-8, Miconazole 23674-86-4, Difluprednate 24169-02-6, Econazole nitrate 25122-46-7, Clobetasol propionate 25322-68-3, Polyethylene glycol 25655-41-8, Povidone Iodine 25717-80-0, Molsidomine 28981-97-7, Alprozolam 29205-06-9, Fluocortolone pivalate 29679-58-1, Fenoprofen 29984-33-6, Vidarabine monophosphate 34580-13-7, Ketotifen 36322-90-4, Piroxicam 36505-84-7, Buspirone 38304-91-5, Minoxidil 39219-28-8, Promestriene 39404-33-6, Dextrates 39809-25-1, Penciclovir 41570-61-0, Tulobuterol 51022-69-6, Amcinonide 52485-79-7, Buprenorphine 53016-31-2,

Norelgestromin 59198-70-8, Diflucortolone Valerate 59227-89-3, Azone 59277-89-3, Acyclovir 60282-87-3, Gestodene 65277-42-1, Ketoconazole 66104-22-1, Pergolide 66734-13-2, Alclometasone dipropionate 72522-13-5, Eptazocine 74103-06-3, Ketonolac 80214-83-1, Roxithromycin 99011-02-6, Imiquimod 99755-59-6, Rotigotine 106685-40-9, Adapalene 113775-47-6, Dexmedetomidine 118292-40-3, Tazarotene 119141-88-7, Esomeprazole 122852-42-0, Alosetron 129722-12-9, Aripiprazole 133099-04-4, Darifenacin 137234-62-9, Voriconazole 141563-69-1, OrZel 143322-58-1, Eletriptan 145158-71-0, Tegaserod 145209-50-3, Thiatolserine 145375-43-5, Mitiglinide 147511-69-1, Pitavastatin 147657-22-5, Calcipotriol monohydrate 153259-65-5, Cilomilast 154189-24-9, Viozan 159776-70-2, Melagatran 163222-33-1 167305-00-2, Omapatrilat 178979-85-6, Capravirine 179463-17-3, Caspofungin acetate 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 202409-33-4, Etoricoxib 287714-41-4, Rosuvastatin 552881-25-1, Crilanomer

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of immediate-release powder in pharmaceutical and nutraceutical compns.)

L61 ANSWER 17 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:473243 HCPLUS Full-text

DOCUMENT NUMBER: 139:41849

TITLE: Pharmaceutical compositions containing a renin inhibitor and antidiabetics

INVENTOR(S): Webb, Randy Lee

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-----------------|
| US 2003114389 | A1 | 20030619 | US 2002-290651 | 20021108 <-- |
| US 2005101638 | A1 | 20050512 | US 2004-14141 | 20041216 <-- |
| US 2007093431 | A1 | 20070426 | US 2006-614401 | 20061221 <-- |
| PRIORITY APPLN. INFO.: | | | US 2001-350708P | P 20011113 <-- |
| | | | US 2002-290651 | B1 20021108 <-- |
| | | | US 2004-14141 | A1 20041216 |

ED Entered STN: 20 Jun 2003

AB The invention relates to a composition comprising a renin inhibitor (e.g., aliskiren) or a salt thereof and at least 1 antidiabetic agent. Thus, a hemifumarate of aliskiren 1000, corn starch 680, colloidal silica 200, Mg stearate 20, stearic acid 50, sodium carboxymethyl starch 250, and water qs to 1000 g.

IC ICM A61K038-04

ICS A61K031-4439; A61K031-426; A61K031-175; A61K031-16

INCL 514019000; 514342000; 514369000; 514592000; 514629000

CC 63-6 (Pharmaceuticals)

ST pharmaceutical antidiabetic renin inhibitor; aliskiren renin inhibitor pharmaceutical

IT Antidiabetic agents

 Diabetes mellitus

 Drug delivery systems

 (pharmaceutical compns. containing renin inhibitor and antidiabetics)

IT Sulfonylureas

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical compns. containing renin inhibitor and
 antidiabetics)

IT Drug delivery systems
 (tablets, coated; pharmaceutical compns. containing renin inhibitor
 and antidiabetics)

IT Drug delivery systems
 (tablets; pharmaceutical compns. containing renin inhibitor and
 antidiabetics)

IT 9015-94-5, Renin, biological studies 54249-88-6, DPP-IV
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitor; pharmaceutical compns. containing renin
 inhibitor and antidiabetics)

IT 89750-14-1, GLP1
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (pharmaceutical compns. containing renin inhibitor and
 antidiabetics)

IT 657-24-9, Metformin 105816-04-4, Nateglinide 111025-46-8, Pioglitazone
 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 145375-43-5
 , Mitiglinide 173334-57-1, Aliskiren 173334-58-2
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical compns. containing renin inhibitor and
 antidiabetics)

IT 9004-10-8, Insulin, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (secretion enhancer; pharmaceutical compns. containing renin
 inhibitor and antidiabetics)

L61 ANSWER 18 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:293592 HCPLUS Full-text
 DOCUMENT NUMBER: 136:325420
 TITLE: Drugs for diabetes, especially type 2,
 comprising an antiinflammatory or analgesic drug,
 selected bivalent linkers, and a nitrate ester
 INVENTOR(S): Del Soldato, Piero
 PATENT ASSIGNEE(S): Nicox S.A., Fr.
 SOURCE: PCT Int. Appl., 66 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

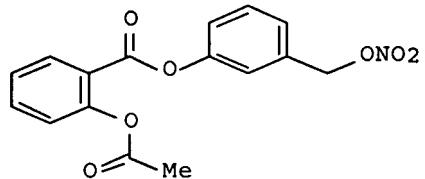
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2002030867 | A2 | 20020418 | WO 2001-EP11665 | 20011009 <-- |
| WO 2002030867 | A3 | 20020725 | | |
| W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ,
EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT,
LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA,
US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| IT 2000MI2201 | A1 | 20020412 | IT 2000-MI2201 | 20001012 <-- |
| IT 1319201 | B1 | 20030926 | | |
| CA 2425655 | A1 | 20020418 | CA 2001-2425655 | 20011009 <-- |
| AU 200214006 | A | 20020422 | AU 2002-14006 | 20011009 <-- |
| EP 1324974 | A2 | 20030709 | EP 2001-982414 | 20011009 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2004511456 T 20040415 JP 2002-534256 20011009 <--
 US 2004023890 A1 20040205 US 2003-398511 20030411 <--
 PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012 <--
 WO 2001-EP11665 W 20011009 <--

OTHER SOURCE(S) : MARPAT 136:325420

ED Entered STN: 19 Apr 2002

GI



- AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)_n-(C)_m-NO₂ [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe²⁺(NH₄)₂(SO₄)₂/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitration of the resultant Ph ester with HNO₃/H₂SO₄ (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.
- IC ICM C07C203-04
 ICS A61K031-04; A61K031-621; A61P003-10
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1
- IT Diabetes mellitus
 (non-insulin-dependent, treatment; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)
- IT 50-81-7, Ascorbic acid, properties 52-67-5, Penicillamine 52-90-4, Cysteine, properties 56-69-9, 5-Hydroxytryptophan 56-84-8, Aspartic acid, properties 57-50-1, Saccharose, properties 60-00-4, Edetic acid, properties 60-24-2, 2-Mercaptoethanol 70-18-8, Glutathione, properties

71-00-1, Histidine, properties 77-92-9, Citric acid, properties
 80-72-8, Reductic acid 89-65-6, Isoascorbic acid 105-59-9,
 N-Methyldiethanolamine 110-15-6, Succinic acid, properties 110-17-8,
 Fumaric acid, properties 110-63-4, 1,4-Butanediol, properties
 111-17-1, 3,3'-Thiodipropionic acid 111-46-6, Diethylene glycol,
 properties 111-48-8, Thiodiethylene glycol 117-39-5, Quercetin
 120-05-8, Sulfuretin 121-34-6, Vanillic acid 121-79-9, Propyl gallate
 123-31-9, Hydroquinone, properties 141-90-2, 2-Thiouracil 149-91-7,
 Gallic acid, properties 154-23-4, Catechin 303-45-7, Gossypol
 305-84-0, L-Carnosine 331-39-5, Caffeic acid 444-27-9,
 4-Thiazolidinecarboxylic acid 458-35-5, Coniferyl alcohol 490-79-9,
 Gentisic acid 500-38-9, Nordihydroguaiaretic acid 501-94-0 520-18-3,
 Kaempferol 520-26-3, Hesperidin 526-84-1, Dihydroxymaleic acid
 533-73-3, Hydroxyhydroquinone 584-85-0, Anserine 591-81-1,
 4-Hydroxybutyric acid 635-65-4, Bilirubin, properties 824-46-4,
 Methoxyhydroquinone 1005-72-7, Tetrahydropyran-2,6-dimethanol
 1077-28-7, Thiocctic acid 1191-25-9, 6-Hydroxyhexanoic acid 1406-18-4,
 Vitamin E 1464-42-2, Selenomethionine 3614-08-2, Selenocysteine
 3690-05-9, p-Cumaric alcohol 6007-86-9, Thiophene-2,5-dimethanol
 7400-08-0, p-Cumaric acid 15537-71-0, N-Acetylpenicillamine
 19750-45-9, 2-Oxo-4-thiazolidinecarboxylic acid 54120-69-3,
 1,4-Dioxan-2,6-dimethanol 54573-75-0, 1 α -OH-Vitamin D2
 55721-11-4, Secalciferol 63147-28-4, 3,5-Di-tert-butyl-4-hydroxybenzyl
 thioglycolate 83805-11-2, Floocalcitriol 92614-59-0, Glutathione ethyl
 ester 97451-46-2, Glutathione isopropyl ester 103909-75-7,
 22-Oxacalcitriol 148258-92-8 326850-58-2, Tetrahydrothiopyran-2,6-
 dimethanol 326850-59-3, 1,4-Dithiane-2,6-dimethanol 326850-60-6,
 Cyclohexene-1,5-dimethanol 326850-61-7, Thiazole-2,5-dimethanol
 326850-62-8, Oxazole-2,5-dimethanol 414355-30-9, 4H-Pyran-2,6-dimethanol
 RL: BSU (Biological study, unclassified); PRP (Properties); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bivalent linker precursor; preparation of antidiabetic agents comprising
 antiinflammatory or analgesic drugs, selected bivalent linkers, and
 nitrate esters)

IT 50-78-2DP, Acetylsalicylic acid, nitroxyl-containing derivs. 61-68-7DP,
 Mefenamic acid, nitroxyl-containing derivs. 65-45-2DP, Salicylamide,
 nitroxyl-containing derivs. 69-72-7DP, Salicylic acid, nitroxyl-containing
 derivs. 89-45-2DP, Salicylsulfuric acid, nitroxyl-containing derivs.
 118-55-8DP, Phenyl salicylate, nitroxyl-containing derivs. 118-57-0DP,
 Acetaminosalol, nitroxyl-containing derivs. 487-48-9DP, Salacetamide,
 nitroxyl-containing derivs. 530-75-6DP, Acetylsalicylsalicylic acid,
 nitroxyl-containing derivs. 530-78-9DP, Flufenamic acid, nitroxyl-containing
 derivs. 552-94-3DP, Salsalate, nitroxyl-containing derivs. 644-62-2DP,
 Meclofenamic acid, nitroxyl-containing derivs. 695-34-1DP,
 2-Amino-4-picoline, nitroxyl-containing derivs. 1503-53-3DP,
 5-Bromosalicylic acid acetate, nitroxyl-containing derivs. 4394-00-7DP,
 Niflumic acid, nitroxyl-containing derivs. 5104-49-4DP, Flurbiprofen,
 nitroxyl-containing derivs. 13710-19-5DP, Tolfenamic acid, nitroxyl-
 containing derivs. 15687-27-1DP, Ibuprofen, nitroxyl-containing derivs. 38194-50-2DP,
 Sulindac, nitroxyl-containing derivs. 38677-85-9DP, Flunixin,
 nitroxyl-containing derivs. 87893-55-8DP, 15-Deoxy- Δ 12,14-
 prostaglandin, nitroxyl-containing derivs. 105816-04-4DP, Nateglinide,
 nitroxyl-containing derivs. 135062-02-1DP, Repaglinide, nitroxyl-containing
 derivs. 145375-43-5DP, Mitiglinide, nitroxyl-containing
 derivs. 177785-17-0DP, (S)-4-[2-(2-Benzoxazolylmethylamino)ethoxy]-
 α -(2,2,2-trifluoroethoxy)benzenepropanoic acid, nitroxyl-containing
 derivs. 195137-72-5DP, JTT-608, nitroxyl-containing derivs. 196808-24-9DP,
 N-(2-Benzoylphenyl)-O-[2-(methyl-2-pyridinylamino)ethyl]-L-tyrosine,

nitroxyl-containing derivs. 196808-45-4DP, Farglitazar, nitroxyl-containing derivs. 236111-01-6DP, (S)-4-[2-(2-Benzoxazolylmethylamino)ethoxy]- α -ethoxybenzenepropanoic acid, nitroxyl-containing derivs. 267412-60-2DP, (2S,5S)-N,N-Dibenzyl-3-[4-(4-Carboxyphenyl)butyl]-2-heptyl-4-oxothiazolidine-5-acetamide, nitroxyl-containing derivs. 403731-62-4DP, Rosiglitazone nitrate, nitroxyl-containing derivs. 414355-31-0DP, Pioglitazone nitrate, nitroxyl-containing derivs.

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidates; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

L61 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:157602 HCAPLUS Full-text

DOCUMENT NUMBER: 136:205430

TITLE: Pharmaceutical compositions containing AT-receptor antagonist or insulin secretion enhancers

INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen

Verwaltungsgesellschaft m.b.H.; Novartis Pharma. GmbH

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 2002015933 | A2 | 20020228 | WO 2001-EP9587 | 20010820 |
| WO 2002015933 | A3 | 20030814 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001087698 | A5 | 20020304 | AU 2001-87698 | 20010820 |
| EP 1351683 | A2 | 20031015 | EP 2001-967289 | 20010820 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004514654 | T | 20040520 | JP 2002-520854 | 20010820 |
| US 2004034065 | A1 | 20040219 | US 2003-362340 | 20030616 |
| US 2006089389 | A1 | 20060427 | US 2005-295928 | 20051207 |
| US 2006281790 | A1 | 20061214 | US 2006-508353 | 20060823 |
| PRIORITY APPLN. INFO.: | | | US 2000-643641 | A 20000822 |
| | | | US 2000-327553P | P 20000822 |
| | | | WO 2001-EP9587 | W 20010820 |
| | | | US 2003-362340 | B1 20030616 |
| | | | US 2005-295928 | B1 20051207 |

ED Entered STN: 01 Mar 2002

AB A pharmaceutical composition comprises as active ingredients an AT1-receptor antagonist or a salt, an insulin secretion enhancer or a its salt or an insulin sensitizer or its salt. Thus, tablets contained Starlix DS 60,

lactose monohydrate 141.5, microcryst. cellulose 71, Povidone-K30 12, and Croscarmellose sodium 18.4, colloidal SiO₂ 6.4, Mg stearate 5.7, and Opadry 9 mg.

IC ICM A61K045-00
 CC 63-6 (Pharmaceuticals)
 IT Angiotensin receptor antagonists
 Antiangular agents
 Antidiabetic agents
 Antihypertensives
 Antiobesity agents
 Cardiovascular agents
 Cataract
 Connective tissue, disease
 Hyperglycemia
 Hypertriglyceridemia
 Hypolipemic agents
 Skin, disease
 (pharmaceutical compns. containing AT-receptor antagonist or insulin secretion enhancers)
 IT 339-43-5, Carbutamide 451-71-8, Glyhexamide 535-65-9, Glybutiazole 631-27-6, Glyclopypyramide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybzole 3149-00-6, Phenbutamide 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 9004-10-8, Insulin, biological studies 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 93479-97-1, Glimepiride 105816-04-4, Nateglinide 114798-26-4, Losartan 133040-01-4, Eprosartan 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139481-59-7, Candesartan 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145375-43-5, Mitiglinide 145733-36-4, Tasosartan
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical compns. containing AT-receptor antagonist or insulin secretion enhancers)

L61 ANSWER 20 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:157564 HCPLUS Full-text
 DOCUMENT NUMBER: 136:205424
 TITLE: Combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors
 INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Novartis Pharma GmbH
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2002015892 | A2 | 20020228 | WO 2001-EP9586 | 20010820 <-- |
| WO 2002015892 | A3 | 20030904 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, | | | | |

PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 US, UZ, VN, YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
 KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
 IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
 GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2002014952 A5 20020304 AU 2002-14952 20010820 <--
 EP 1359907 A2 20031112 EP 2001-983442 20010820 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2004519424 T 20040702 JP 2002-520813 20010820 <--
 US 2004087630 A1 20040506 US 2003-362341 20030618 <--
 PRIORITY APPLN. INFO.: US 2000-643642 A 20000822 <--
 WO 2001-EP9586 W 20010820 <--

ED Entered STN: 01 Mar 2002

AB The present invention relates to a combination, especially a pharmaceutical composition, comprising (a) an insulin secretion enhancer or a pharmaceutically acceptable salt thereof and (b) at least one of the active ingredients selected from the group consisting of (i) HMG-Co-A reductase inhibitors or a pharmaceutically acceptable salt thereof; and (ii) ACE inhibitors or a pharmaceutically acceptable salt thereof; and, in case of a pharmaceutical composition, a pharmaceutically acceptable carrier. Formulations were given as examples, e.g., tablets containing nateglinide.

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST insulin secretion enhancer pharmaceutical combination; HMG CoA reductase inhibitor pharmaceutical combination; acetylcholinesterase inhibitor pharmaceutical combination

IT Antidiabetic agents

Antihypertensives

Antiobesity agents

Connective tissue, disease

Eye, disease

Hypolipemic agents

Skin, disease

(combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Nerve, disease

(diabetic neuropathy; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Eye, disease

(diabetic retinopathy; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Heart, disease

(failure; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Kidney, disease

(glomerulosclerosis; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Sexual disorders

(impotence; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT Eye, disease

(macula, degeneration; combinations of insulin secretion enhancer,

- HMG-CoA reductase inhibitors and
acetylcholinesterase inhibitors)
- IT Inflammation
Intestine, disease
(ulcerative colitis; combinations of insulin secretion enhancer,
HMG-CoA reductase inhibitors and
acetylcholinesterase inhibitors)
- IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combinations of insulin secretion enhancer, HMG-CoA reductase
inhibitors and acetylcholinesterase inhibitors)
- IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide
339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole
631-27-6, Glyclopypyramide 664-95-9, Tolcyclamide 968-81-0,
Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide
1492-02-0, Glybzole 3149-00-6, Phenbutamide 4618-41-1,
1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 21187-98-4,
Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride
29094-61-9, Glipizide 33342-05-1, Gliquidone 62571-86-2, Captopril
74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril
76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin
81093-37-0, Pravastatin 82834-16-0, Perindopril 83435-66-9, Delapril
83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril
86541-75-5, Benazepril 86541-78-8, Benazeprilat 87333-19-5, Ramipril
87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril
93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril
105816-04-4, Nateglinide 111223-26-8, Ceronapril 111902-57-9,
Temocapril 134523-00-5, Atorvastatin 135062-02-1, Repaglinide
145375-43-5, Mitiglinide 145599-86-6, Cerivastatin
147511-69-1, Pitavastatin 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of insulin secretion enhancer, HMG-CoA reductase
inhibitors and acetylcholinesterase inhibitors)
- IT 9000-81-1, Acetylcholinesterase 9028-35-7, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; combinations of insulin secretion enhancer,
HMG-CoA reductase inhibitors and
acetylcholinesterase inhibitors)

L61 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2002:51257 HCAPLUS Full-text
 DOCUMENT NUMBER: 136:123595
 TITLE: A combination of phosphonate or phosphorodiamidate
FBPase inhibitors and antidiabetic agents
useful for the treatment of diabetes
 INVENTOR(S): Van Poelje, Paul D.; Erion, Mark D.; Fujiwara,
Toshihiko
 PATENT ASSIGNEE(S): Metabasis Therapeutics, Inc., USA; Sankyo Company,
Ltd.
 SOURCE: PCT Int. Appl., 392 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|-------|----------|-----------------|--------------|
| ----- | ----- | ----- | ----- | ----- |
| WO 2002003978 | A2 | 20020117 | WO 2001-US21557 | 20010705 <-- |
| WO 2002003978 | A3 | 20031016 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GW, ML, MR, NE, SN, TD, TG

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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004508297 | T | 20040318 | JP 2002-508433 | 20010705 <-- |
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| NO 2003000034 | A | 20030305 | NO 2003-34 | 20030103 <-- |
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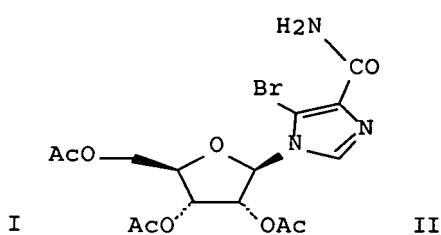
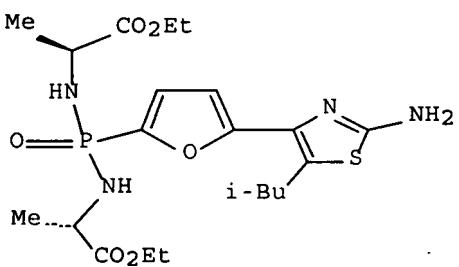
PRIORITY APPLN. INFO.:

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ED Entered STN: 18 Jan 2002

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AB A combination therapy of at least one FBPase inhibitor ((R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M; e.g. 2-amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide and 2-amino-5-isobutyl-4-[2-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-5-furanyl]thiazole (shown as I)) and at least one other antidiabetic agent (insulin secretagogue; e.g. glyburide, a sulfonylurea) is disclosed. (R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M are converted in vivo or in vitro to MPO32-, which inhibit FBPase; the substituents are defined in the claims. General methods and about 15 specific example preps. of the phosphorus

compds. are included but no methods of preparation are claimed. In the biol. examples, data is presented for the following for selected phosphorus compds. and other materials: inhibition of human liver FBPase, inhibition of rat liver and mouse liver FBPase, inhibition of gluconeogenesis by an FBPase inhibitor in rat hepatocytes, inhibition of glucose production and elevation of fructose-1,6-bisphosphate levels in rat hepatocytes treated with FBPase inhibitors, anal. of hepatic and plasma drug metabolite levels, blood glucose, and hepatic fructose 1,6-bisphosphate levels after administration of compound A (shown as II) p.o. to normal fasted rats, anal. of hepatic and plasma drug levels after administration of compds. i.p. to normal fasted rats, oral bioavailability determination of two compds. and oral glucose lowering activity of two compds. For insulin secretagogues: insulin release from pancreatic islets, glucose lowering in the fasted rat, i.v. glucose tolerance in the fasted rat, oral glucose tolerance in the Zucker diabetic fatty rat, insulin secretion in the rat, inhibition of KATP-channels in mouse pancreatic beta-cells, and sulfonylurea receptor binding. Also included are: inhibition of dipeptidyl peptidase IV (DPP-IV inhibitors), alpha-glucosidase assay, glycogen phosphorylase assay, assay of glucose 6-phosphatase inhibitors, glucagon antagonist assay, amylin agonist assay, fatty acid oxidation inhibitor assay, glucose lowering in the db/db mouse (FBPase inhibitor), glucose lowering in the ZDF rat, acute combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, chronic combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, acute combination treatment of insulin and an FBPase inhibitor in db/db mice, beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db mice, and beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db Mice. Also included are: acute combination treatment of insulin and an FBPase inhibitor in the Goto-Kakizaki rat, acute combination treatment of a biguanide and an FBPase inhibitor in db/db mice, acute combination treatment of an alpha glucosidase inhibitor and an FBPase inhibitor in Goto-Kakizaki rats, acute combination treatment of a glycogen phosphorylase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of a glucose-6-phosphatase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of an FBPase inhibitor and an amylin agonist, chronic combination treatment of a fatty acid oxidation inhibitor and an FBPase inhibitor in the streptozotocin-induced diabetic rat.

- IC ICM A61K031-00
 CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 1, 27, 28, 29
 ST antidiabetic agent phosphonate phosphorodiamidate FBPase inhibitor diabetes treatment; insulin secretagogue phosphonate phosphorodiamidate FBPase inhibitor diabetes treatment
 IT Potassium channel
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (ATP-sensitive; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
 IT Glucagon-like peptide-1 receptors
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (agonists; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
 IT Sulfonylurea receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (binding; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
 IT Antiobesity agents

- (combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful as)
- IT Antidiabetic agents
 B cell (lymphocyte)
 Drug bioavailability
 Human
 Pancreatic islet of Langerhans
 (combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Antioxidants
 (fatty acid; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Liver
 (fructose bisphosphatase of; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Liver
 (hepatocyte, fructose bisphosphatase of; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Gluconeogenesis
 (inhibitors; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Fatty acids, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Sulfonylureas
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (insulin secretagogues; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Drug delivery systems
 (oral; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Organic compounds, biological studies
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (phosphorus-containing; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT Drug delivery systems
 (prodrugs; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 106602-62-4, Amylin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (agonists; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 151126-32-8, Pramlintide
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amylin agonist; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)

- IT 9007-92-5, Glucagon, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 50-99-7, D-Glucose, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (blood; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 213125-12-3P, 5-Diethylphosphono-2-(4-methyl-1-oxopentyl)furan
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 261365-06-4P, 5-Diethylphosphono-2-acetyl furan 261365-08-6P, 5-Diethylphosphono-2-(1-oxobutyl)furan 261365-11-1P, 2-Amino-5-isobutyl-4-[5-phosphono-2-furanyl]thiazole 261365-17-7P, 261365-19-9P, 2-Methyl-4-(5-phosphono-2-furanyl)thiazole 261365-23-5P, 2-Isopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-25-7P, 5-Isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-27-9P, 2-Aminothiocarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-31-5P, 261365-33-7P, 2-(2-Thienyl)-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-36-0P 261365-37-1P, 2-Acetamido-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-38-2P, 2-Amino-4-(5-phosphono-2-furanyl)thiazole 261365-40-6P, 2-Methylamino-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-44-0P 261365-48-4P 261365-51-9P 261365-55-3P 261365-56-4P, 2-Ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-58-6P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261365-60-0P, 2-Cyanomethyl-4-(5-phosphono-2-furanyl)thiazole 261365-62-2P, 261365-63-3P, 2-Amino-5-propyl-4-(5-phosphono-2-furanyl)thiazole 261365-65-5P 261365-66-6P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole 261365-67-7P, 2-Amino-5-cyclopropyl-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261365-68-8P, 2-Amino-5-cyclopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-70-2P, 2-Amino-5-benzylloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-72-4P, 261365-73-5P, 2-Amino-5-[N,N-dimethylaminomethyl]-4-(5-phosphono-2-furanyl)thiazole dihydrobromide 261365-75-7P, 2-Amino-5-methoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-78-0P, 2-Amino-5-propyloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-79-1P, 2-Amino-5-benzyl-4-(5-phosphono-2-furanyl)thiazole 261365-80-4P, 2-Amino-5-[N,N-diethylaminomethyl]-4-(5-phosphono-2-furanyl)thiazole dihydrobromide 261365-83-7P, 2-Amino-5-(N,N-dimethylcarbamoyl)-4-(5-phosphono-2-furanyl)thiazole 261365-85-9P, 2-Amino-5-carboxy-4-(5-phosphono-2-furanyl)thiazole 261365-86-0P, 2-Amino-5-isopropyloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-89-3P, 2-Methyl-5-cyclopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-90-6P, 2-Methyl-5-ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-92-8P, 2-[N-Acetyl amino]-5-methoxymethyl-4-(5-phosphono-2-furanyl)thiazole 261365-95-1P, 2-Amino-5-cyclopropylmethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-98-4P, 2-[(N-Dansyl)amino]-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-99-5P, 2-Amino-5-(2,2,2-trifluoroethyl)-4-(5-phosphono-2-furanyl)thiazole 261366-00-1P, 2-Methyl-5-methylthio-4-(5-phosphono-2-furanyl)thiazole 261366-01-2P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole

monoammonium salt 261366-02-3P, 2-Cyano-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261366-03-4P, 2-Amino-5-hydroxymethyl-4-(5-phosphono-2-furanyl)thiazole 261366-05-6P, 2-Cyano-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-06-7P, 2-Amino-5-isopropylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261366-07-8P, 2-Amino-5-phenylthio-4-(5-phosphono-2-furanyl)thiazole 261366-08-9P, 2-Amino-5-tert-butylthio-4-(5-phosphono-2-furanyl)thiazole 261366-09-0P, 2-Amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261366-11-4P, 2-Amino-5-ethylthio-4-(5-phosphono-2-furanyl)thiazole 261366-12-5P, 2-[N-(tert-Butyloxycarbonyl)amino]-5-methoxymethyl-4-(5-phosphono-2-furanyl)thiazole 261366-13-6P, 2-Hydroxy-4-(5-phosphono-2-furanyl)thiazole 261366-14-7P, 2-Hydroxy-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261366-16-9P, 2-Hydroxy-5-isopropyl-4-(5-phosphono-2-furanyl)thiazole 261366-17-0P, 2-Hydroxy-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-18-1P, 5-Ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261366-20-5P, 2-Amino-5-vinyl-4-(5-phosphono-2-furanyl)thiazole 261366-21-6P, 2-Methylthio-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-24-9P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)selenazole 261366-26-1P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)selenazole 261366-40-9P, 2-Amino-5-(2-furanyl)-4-(5-phosphono-2-furanyl)thiazole 261366-65-8P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole 261366-66-9P, 2-Hydroxy-5-isobutyl-4-(5-phosphono-2-furanyl)imidazole 261366-67-0P, 2-Methyl-4-isobutyl-5-(5-phosphono-2-furanyl)oxazole monohydrobromide 261366-68-1P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole monohydrobromide 261366-69-2P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)imidazole monohydrobromide 261366-71-6P, 2-Trifluoromethyl-4-(5-phosphono-2-furanyl)imidazole 261366-73-8P, 4,5-Dimethyl-1-isobutyl-2-(5-phosphono-2-furanyl)imidazole 261366-74-9P, 2-Amino-5-propyl-4-(5-phosphono-2-furanyl)oxazole 261366-75-0P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)oxazole 261366-76-1P, 2-Amino-5-methyl-4-(5-phosphono-2-furanyl)oxazole 261366-77-2P, 2-Amino-4-(5-phosphono-2-furanyl)oxazole 261366-78-3P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole monohydrobromide 261370-26-7P 261370-27-8P, 2-Methyl-5-isobutyl-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-29-0P, 2-Amino-5-methylthio-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-30-3P, 2-Amino-5-isobutyl-4-(5-phosphonomonoamido-2-furanyl)thiazole 261370-31-4P, 2-Amino-5-isobutyl-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-32-5P, 2-Amino-5-isobutyl-4-[5-(N,N'-diisobutylphosphorodiamido)-2-furanyl]thiazole 261370-33-6P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1,3-bis(ethoxycarbonyl)-1-propyl]phosphorodiamido]-2-furanyl]thiazole 261370-34-7P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-benzyloxycarbonylethyl)phosphorodiamido]-2-furanyl]thiazole 261370-35-8P 261370-39-2P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1-methoxycarbonylethyl)phosphonamido]-2-furanyl]thiazole 261370-44-9P, 2-Amino-5-isobutyl-4-[5-(O-phenylphosphonamido)-2-furanyl]thiazole 261370-46-1P, 2-Amino-5-isobutyl-4-(5-(O-phenyl-N-ethoxycarbonylmethylphosphonamido)-2-furanyl)thiazole 261370-48-3P, 2-Amino-5-isobutyl-4-(5-(O-phenyl-N-isobutylphosphonamido)-2-furanyl)thiazole 261370-50-7P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1-ethoxycarbonyl-2-phenylethyl)phosphonamido]-2-furanyl]thiazole 261370-54-1P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1,3-bis(ethoxycarbonyl)propyl)phosphonamido]-2-furanyl]thiazole 261370-57-4P, 2-Amino-5-isobutyl-4-[5-[O-(3-chlorophenyl)-N-((S)-1-(methoxycarbonyl)ethyl)phosphonamido]-2-furanyl]thiazole 261370-60-9P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[1,1-bis(ethoxycarbonyl)methyl]phosphonamido]-2-furanyl]thiazole 261370-61-0P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-(1-morpholinyl)phosphonamido]-2-furanyl]thiazole 261370-62-1P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1-(benzyloxycarbonyl)ethyl)phosphonamido]-2-furanyl]thiazole 261370-63-2P, 2-Amino-5-isobutyl-4-(5-(O-

phenyl-N-benzyloxycarbonylmethylphosphonamido)-2-furanyl)thiazole
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 261370-69-8P 261370-70-1P 261370-71-2P 261370-73-4P 261370-74-5P
 261370-76-7P, 2-Amino-5-methylthio-4-(5-(N-methyl-1-phenyl-1,3-propylphosphonamido)-2-furanyl)thiazole 261370-79-0P,
 2-Amino-5-isobutyl-4-[5-[3-(3,5-dichlorophenyl)-1,3-propyl]phosphonamido]-2-furanyl]thiazole 261370-80-3P, 2-Amino-5-isobutyl-4-[5-(4,5-benzo-1-oxo-1-phospho-2-oxa-6-azacyclohexan-1-yl)-2-furanyl]thiazole
 261372-35-4P, 2-Amino-4-phosphonomethoxy-6-bromobenzothiazole
 261372-36-5P, 2-Amino-4-phosphonomethoxybenzothiazole 261372-38-7P,
 2-Amino-4-phosphonomethoxy-6-bromo-7-chlorobenzothiazole 261372-39-8P,
 2-Amino-4-phosphonomethoxy-6-bromo-7-methylbenzothiazole 261372-40-1P,
 2-Amino-4-phosphonomethoxy-7-methylbenzothiazole 261372-42-3P,
 2-Amino-4-phosphonomethoxy-7-chlorobenzothiazole 261372-64-9P,
 2-Amino-7-ethyl-6-thiocyanato-4-phosphonomethoxybenzothiazole
 261373-40-4P, 2-Methyl-5-ethyl-4-(5-phosphono-2-furanyl)thiazole
 280779-70-6P, 2-Phenyl-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole
 280779-71-7P, 2-Amino-5-isopropyl-4-(5-phosphono-2-furanyl)thiazole
 280779-72-8P; 2-Amino-5-methanesulfinyl-4-(5-phosphono-2-furanyl)thiazole
 280779-74-0P, 2-Amino-5-(4-morpholinyl)methyl-4-(5-phosphono-2-furanyl)thiazole dihyd robromide 280779-79-5P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)selenazole 280779-91-1P, 2-Vinyl-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 280782-95-8P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis(benzyloxycarbonylmethyl)phosphonodiamido]furanyl]-2-thiazole
 280782-96-9P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(R)-1-(methoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole
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 280783-00-8P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(1-methyl-1-ethoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole 280783-01-9P,
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 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(R)-1-ethoxycarbonyl-2-(benzylthio)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-06-4P,
 2-Amino-5-propylthio-4-[5-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-07-5P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-benzyloxycarbonyl-2-methylisobutyl]phosphonodiamido]-2-furanyl]thiazole 280783-08-6P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-3-methylbutyl]phosphonodiamido]-2-furanyl]thiazole
 280783-09-7P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-2-methylpropyl]phosphonodiamido]-2-furanyl]thiazole 280783-10-0P,
 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-2-phenylethyl]phosphonodiamido]-2-furanyl]thiazole 280783-11-1P,
 2-Amino-5-propylthio-4-[5-[N,N'-bis[(1-methyl-1-ethoxycarbonylethyl)phosphonodiamido]-2-furanyl]]thiazole 280783-12-2P,
 2-Amino-5-methylthio-4-[5-[N,N'-bis[1-methyl-1-ethoxycarbonylethyl]phosphonodiamido]-2-furanyl]thiazole 280783-13-3P,
 2-Amino-5-isobutyl-4-[5-[N-morpholino-N'-[1-methyl-1-ethoxycarbonylethyl]phosphonodiamido]-2-furanyl]thiazole 280783-14-4P,
 2-Amino-5-isobutyl-4-[5-[N-pyrrolidino-N'-[1-methyl-1-ethoxycarbonylethyl]phosphonodiamido]-2-furanyl]thiazole 347870-21-7P,
 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonylpropyl]phosphorodiamido]-2-furanyl]thiazole

ido]-2-furanyl]thiazole 347870-33-1P, 2-Amino-5-(2-thienyl)-4-(5-diethylphosphono-2-furanyl)thiazole 358670-36-7P, (5-(3,5-Dinitrophenyl)-2-furanyl)phosphonic acid 358670-37-8P, (5-(2-Amino-3,5-dinitrophenyl)-2-furanyl)phosphonic acid 358670-38-9P, (5-(5-Chloro-2-methoxyphenyl)-2-furanyl)phosphonic acid 358670-39-0P, (5-(2,5-Dichlorophenyl)-2-furanyl)phosphonic acid 358670-40-3P, (5-(2-Methylsulfamoyl-5-(trifluoromethyl)phenyl)-2-furanyl)phosphonic acid 358670-41-4P, (5-(5-Chloro-2-(methylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-42-5P, (5-(2-(Methylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-44-7P, (5-(2-Hydroxyphenyl)-2-furanyl)phosphonic acid 358670-45-8P, (5-(3,5-Dimethylphenyl)-2-furanyl)phosphonic acid 358670-46-9P, (5-(3-Bromophenyl)-2-furanyl)phosphonic acid 358670-47-0P, (5-(4-Aminophenyl)-2-furanyl)phosphonic acid 358670-48-1P, (5-(4-Chloro-2,5-dimethoxyphenyl)-2-furanyl)phosphonic acid 358670-49-2P, (5-(2-(4-Chlorobenzyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-50-5P, (5-(2-(2-(4-Chlorophenyl)ethyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-51-6P, (5-(2-(Benzylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-52-7P, (5-(2-Sulfamoylphenyl)-2-furanyl)phosphonic acid 358670-53-8P, (5-Pentamethylphenyl-2-furanyl)phosphonic acid 358670-54-9P, (5-(2,3-Dicarboethoxyphenyl)-2-furanyl)phosphonic acid 358670-56-1P, (5-(4-Acetylamino-3-methylphenyl)-2-furanyl)phosphonic acid 358670-58-3P, (5-(2,4-Dichloro-6-methylphenyl)-2-furanyl)phosphonic acid 358670-59-4P, (5-(4-Hydroxy-2-carbomethoxyphenyl)-2-furanyl)phosphonic acid 358670-60-7P, (5-(2-Carbamoyl-4-methylphenyl)-2-furanyl)phosphonic acid 358670-61-8P, (5-(2-Ethoxycarbonyl-4-hydroxyphenyl)-2-furanyl)phosphonic acid 358670-62-9P, (5-(4-Nitrophenyl)-2-furanyl)phosphonic acid 358670-63-0P, (5-(2-(2,4-Difluorophenyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-64-1P, (5-(3,5-Dichlorophenyl)-2-furanyl)phosphonic acid 358670-65-2P, (5-(3-Hydroxyphenyl)-2-furanyl)phosphonic acid 358670-66-3P, (5-(5-Bromo-3-carboxyphenyl)-2-furanyl)phosphonic acid 358670-67-4P, (5-(5-Formyl-2,3-dimethoxyphenyl)-2-furanyl)phosphonic acid 358670-68-5P, (5-(2-Nitrophenyl)-2-furanyl)phosphonic acid 358670-69-6P, (5-(Biphenyl-2-yl)-2-furanyl)phosphonic acid 358670-70-9P, (5-(2-(Carboethoxy)phenyl)-2-furanyl)phosphonic acid 358670-71-0P, (5-(4-Bromophenyl)-2-furanyl)phosphonic acid 358670-72-1P, (5-(3-Propanoylphenyl)-2-furanyl)phosphonic acid 358670-73-2P, (5-(5-Cyano-2-methoxyphenyl)-2-furanyl)phosphonic acid 358670-74-3P, (5-(2-Ethylphenyl)-2-furanyl)phosphonic acid 358670-75-4P, (5-(6-Methyl-2-nitrophenyl)-2-furanyl)phosphonic acid 358670-76-5P, (5-(4-(Acetylamino)phenyl)-2-furanyl)phosphonic acid 358670-77-6P, (5-(2,3,4,5-Tetramethylphenyl)-2-furanyl)phosphonic acid 358670-78-7P, (5-(Biphenyl-3-yl)-2-furanyl)phosphonic acid 358670-79-8P, (5-(5-Chloro-2-sulfamoylphenyl)-2-furanyl)phosphonic acid 358670-80-1P, (5-(4-(((1-Pyrrolidinyl)acetyl)amino)phenyl)-2-furanyl)phosphonic acid 358670-81-2P, (5-(3,4-Dimethylphenyl)-2-furanyl)phosphonic acid 358670-82-3P, (5-(2,4-Dinitrophenyl)-2-furanyl)phosphonic acid 358670-83-4P, (5-(3-(Aminomethyl)phenyl)-2-furanyl)phosphonic acid 358670-84-5P, (5-(4-Amino-3-fluorophenyl)-2-furanyl)phosphonic acid 358670-85-6P, (5-(3-(Hydroxymethyl)phenyl)-2-furanyl)phosphonic acid 358670-86-7P, (5-(2-Bromophenyl)-2-furanyl)phosphonic acid 358670-87-8P, (5-(2-(2-Hydroxyethyl)phenyl)-2-furanyl)phosphonic acid 358670-88-9P, (5-(4-Carbamoylphenyl)-2-furanyl)phosphonic acid 358670-89-0P, (5-(4-Cyanophenyl)-2-furanyl)phosphonic acid 358670-90-3P, (5-(3-Cyanophenyl)-2-furanyl)phosphonic acid 358670-91-4P, (5-(2-Cyanophenyl)-2-furanyl)phosphonic acid 358670-92-5P, (5-(4-Amino-3-nitrophenyl)-2-furanyl)phosphonic acid 358670-93-6P, (5-(2-Isopropylphenyl)-2-furanyl)phosphonic acid 358670-94-7P, (5-(6-Amino-2-chloro-3-pyridyl)-2-furanyl)phosphonic acid 358670-95-8P,

(5-(2-Amino-5-chlorophenyl)-2-furanyl)phosphonic acid 358670-96-9P,
 (5-(3-Chloro-5-fluorophenyl)-2-furanyl)phosphonic acid 358670-97-0P,
 (5-(2-Methyl-5-nitrophenyl)-2-furanyl)phosphonic acid 358670-98-1P,
 (5-(5-Fluoro-3-nitrophenyl)-2-furanyl)phosphonic acid 358670-99-2P,
 (5-(2-Amino-5-carbomethoxyphenyl)-2-furanyl)phosphonic acid
 358671-00-8P, (5-(2-Methoxy-5-nitrophenyl)-2-furanyl)phosphonic acid
 358671-01-9P, (5-(2-Chloro-5-(trifluoromethyl)phenyl)-2-furanyl)phosphonic acid
 358671-02-0P, (5-(2,5-Bis(trifluoromethyl)phenyl)-2-furanyl)phosphonic acid
 358671-03-1P, (5-(4-Fluorophenyl)-2-furanyl)phosphonic acid
 358671-04-2P, (5-(2,4-Dichlorophenyl)-2-furanyl)phosphonic acid
 358671-05-3P, (5-(3-Amino-5-carbomethoxyphenyl)-2-furanyl)phosphonic acid
 358671-06-4P, (5-(3-Amino-4-bromophenyl)-2-furanyl)phosphonic acid
 358672-11-4P, (5-(4-Methyl-3-thienyl)-2-furanyl)phosphonic acid
 389057-32-3P, (5-(2-(Propylsulfamoyl)phenyl)-2-furanyl)phosphonic acid
 389057-53-8P 389057-54-9P,
 2-Amino-5-ethylthiocarbonyl-4-(5-phosphono-2-furanyl)thiazole
 389057-55-0P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole
 N,N-dicyclohexylammonium salt 389057-73-2P, 2-Amino-5-isobutyl-4-[5-[O-(4-chlorophenyl)-N-((S)-1-methoxycarbonylethyl)phosphonamido]-2-furanyl]thiazole 389057-74-3P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[2-(ethoxycarbonyl)propyl]phosphonamido]-2-furanyl]thiazole 389057-76-5P,
 2-Amino-4-[[3-(3,5-dichlorophenyl)propane-1,3-diyl]phosphonometoxy]-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)

- IT 213124-93-7 213199-10-1 213247-37-1 240434-61-1 280783-15-5
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 213190-65-9, Exendin
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (exendin and exendin agonists, insulin secretagogue; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 9004-10-8, Insulin, biological studies 116094-23-6, Insulin aspart
 133107-64-9, Insulin lispro 160337-95-1, Insulin glargine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (in combination with phosphonate or phosphorodiamidate FBPase inhibitors useful for treatment of diabetes)
- IT 9001-39-2, Glucose-6-phosphatase 9001-42-7, α -Glucosidase
 9001-52-9, Fructose bisphosphatase 9035-74-9, Glycogen phosphorylase
 54249-88-6, Dipeptidyl peptidase-IV
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)
- IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin
 451-71-8, Glyhexamide 657-24-9, Metformin 664-95-9, Tolcyclamide
 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide
 3149-00-6, Phenbutamide 10238-21-8, Glyburide 21187-98-4, Gliclazide
 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide
 33342-05-1, Gliquidone 56180-94-0, Acarbose 72432-03-2, Miglitol

- 83480-29-9, Voglibose 93479-97-1, Glimepiride 105816-04-4, Nateglinide
 135062-02-1, Repaglinide 145375-43-5, Mitiglinide
 161748-40-9, BTS-67582 204656-20-2, NN 2211 247016-69-9, NVP-DPP728
 251572-86-8, P 32/98
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (insulin secretagogue; combination of phosphonate or phosphorodiamidate
 FBPase inhibitors and antidiabetic agents useful for
 treatment of diabetes)
- IT 261373-15-3P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); RACT (Reactant or reagent); USES (Uses)
 (intermediate; combination of phosphonate or phosphorodiamidate FBPase
 inhibitors and antidiabetic agents useful for treatment of
 diabetes)
- IT 1738-68-7, Benzyl aminoacetate 358672-65-8, 6-Amino-2-chloro-3-
 bromopyridine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (intermediate; combination of phosphonate or phosphorodiamidate FBPase
 inhibitors and antidiabetic agents useful for treatment of
 diabetes)
- IT 36366-55-9P, Diethyl 2-furanylphosphonate 78072-59-0P,
 2-(4-Methyl-1-oxopentyl)furan 82619-14-5P, Ethoxycarbonyloxymethyl
 iodide 104208-14-2P 213124-94-8P, 5-Diethylphosphono-2-furaldehyde
 261372-78-5P, 2-Bromo-5-isobutyl-4-(5-diethylphosphono-2-furanyl)thiazole
 261373-31-3P, 2-Diethylphosphonomethyloxy-5-bromonitrobenzene
 389057-77-6P, 4-Phosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole
 dichloride
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (intermediate; combination of phosphonate or phosphorodiamidate FBPase
 inhibitors and antidiabetic agents useful for treatment of
 diabetes)
- IT 953-18-4P, (R)-Ethyl 2-amino-3-(benzylthio)propanoate 2666-93-5P,
 L-Leucine methyl ester 2743-60-4P, L-Leucine ethyl ester 3081-24-1P,
 L-Phenylalanine ethyl ester 13200-60-7P, N-Methylglycine ethyl ester
 17431-03-7P, L-Valine ethyl ester 21760-98-5P, L-Valine benzyl ester
 154092-64-5P, (S)-Benzyl 2-amino-3,3-dimethylbutanoate
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (reactant; combination of phosphonate or phosphorodiamidate FBPase
 inhibitors and antidiabetic agents useful for treatment of
 diabetes)
- IT 78-81-9, Isobutylamine 88-67-5, 2-Iodobenzoic acid 98-01-1,
 2-Furaldehyde, reactions 109-80-8, 1,3-Propanedithiol 110-00-9, Furan
 110-70-3, N,N'-Dimethylmethylenediamine 354-37-0, Trifluoroacetamidine
 431-03-8, 2,3-Butanedione 459-73-4, Glycine ethyl ester 533-58-4,
 2-Iodophenol 540-37-4, 4-Iodoaniline 583-55-1, 2-Bromo-1-iodobenzene
 589-87-7, 1-Bromo-4-iodobenzene 591-18-4, 1-Bromo-3-iodobenzene
 609-73-4, 1-Iodo-2-nitrobenzene 622-50-4, 4-Iodoacetanilide 623-00-7,
 4-Bromobenzonitrile 626-02-8, 3-Iodophenol 636-98-6,
 1-Iodo-4-nitrobenzene 646-07-1, 4-Methylpentanoic acid 672-57-1,
 2-Chloro-1-ido-5-trifluoromethylbenzene 696-40-2, 3-Iodobenzylamine
 709-49-9, 1-Iodo-2,4-dinitrobenzene 814-49-3, Diethyl chlorophosphate
 873-38-1, 2-Bromo-4-chloroaniline 875-51-4, 4-Bromo-2-nitroaniline
 1074-16-4, 2-Bromophenethyl alcohol 1113-49-1, Ethyl
 2-amino-2-methylpropanoate 1115-59-9, L-Alanine ethyl ester,
 hydrochloride 1459-01-4, 2-Iodoisopropylbenzene 1765-93-1,

4-Fluorophenylboronic acid 1817-73-8, 2-Bromo-4,6-dinitroaniline
 2042-37-7, 2-Bromobenzonitrile 2113-51-1, 2-Iodobiphenyl 2113-57-7,
 3-Bromobiphenyl 2491-20-5, L-Alanine methyl ester hydrochloride
 3032-81-3, 3,5-Dichloroiodobenzene 3082-75-5, L-Alanine ethyl ester
 3819-88-3, 3-Nitro-5-fluoro-1-iodobenzene 3853-91-6,
 1-Iodo-2,3,4,5,6-pentamethylbenzene 3956-07-8, 4-Iodobenzamide
 5197-28-4, 2-Bromo-4-nitroanisole 5464-79-9, 2-Amino-4-
 methoxybenzothiazole 6456-74-2 6937-34-4, 3-Iodophthalic acid
 6948-30-7, 3-Bromo-4,5-dimethoxybenzaldehyde 6952-59-6,
 3-Bromobenzonitrile 7051-34-5, Cyclopropanemethyl bromide 7617-93-8,
 1-Bromo-2,5-bis(trifluoromethyl)benzene 7745-93-9, 2-Bromo-4-
 nitrotoluene 13529-27-6, 2-Furaldehyde diethyl acetal 16450-41-2,
 L-Glutamic acid diethyl ester 17831-01-5, L-Alanine benzyl ester
 18282-40-1, 1-Ethyl-2-iodobenzene 19718-49-1, 2-Iodo-4-
 carbomethoxyaniline 19829-31-3, 3'-Bromopropiophenone 21705-13-5,
 D-Alanine methyl ester 22445-41-6, 5-Iodo-m-xylene 29632-74-4,
 2-Fluoro-4-idoaniline 29682-41-5, 2,5-Dichloro-1-iodobenzene
 30318-99-1, 3-Bromo-4-methylthiophene 31599-61-8, 3,4-
 Dimethyliodobenzene 33863-76-2, 1-Bromo-3-chloro-5-fluorobenzene
 41085-43-2, 2-Bromo-3-nitrotoluene 45644-21-1, 6-Amino-2-chloropyridine
 52807-27-9, 4-Chloro-2-idoanisole 53730-99-7, 2-Iodobenesulfonamide
 54509-71-6, 2,3,4,5-Tetramethyliodobenzene 57455-06-8, 3-Iodobenzyl
 alcohol 57772-57-3, 5-Hydroxy-2-iodobenzoic acid 63980-69-8,
 1-(2-Methoxy-5-chlorophenyl)thiourea 68716-47-2, 2,4-
 Dichlorophenylboronic acid 85006-23-1, 3-Aminophenylboronic acid
 hydrochloride 90064-46-3, 2,5-Dimethoxy-4-iodochlorobenzene
 106938-62-9, Diethylphosphonomethyl trifluoromethylsulfonate
 117324-09-1, 4-Iodo-2-methylacetanilide 117572-79-9,
 3-Bromo-4-methoxybenzonitrile 118486-94-5, 2-Tributylstannylfuran
 125259-03-2, N-Methyl-2-iodobenesulfonamide 175277-97-1,
 3,5-Dichloro-2-iodotoluene 188815-32-9, 3-Bromo-5-iodobenzoic acid
 261369-11-3, 2-Amino-5-isobutyl-4-(5-diphenylphosphono-2-furanyl)thiazole
 261372-76-3, 2-Amino-5-isobutyl-4-(5-diethylphosphono-2-furanyl)thiazole
 261372-77-4, 2-Amino-5-bromo-4-(5-diethylphosphono-2-furanyl)thiazole
 261373-39-1, 3-(3,5-Dichlorophenyl)-1,3-propanediol 270086-79-8,
 N-(4-Iodophenyl)-2-(tetrahydro-1H-pyrrol-1-yl)acetamide 271796-28-2,
 4-Chloro-2-iodobenesulfonamide 271796-61-3, N-Benzyl-2-
 iodobenesulfonamide 271796-68-0, N-Propyl-4-chloro-2-
 iodobenesulfonamide 273208-13-2, N-Methyl-2-iodo-4-
 (trifluoromethyl)benzenesulfonamide 273208-16-5, N-Methyl-4-chloro-2-
 iodobenesulfonamide 304644-56-2, N-(4-Chlorobenzyl)-2-iodobenzamide
 309253-36-9, 2-Iodo-5-methylbenzamide 347869-08-3, 5-Diethylphosphono-2-
 (2-bromo-4-methyl-1-oxopentyl)furan 347869-10-7, 5-Diethylphosphono-2-
 (bromoacetyl)furan 347869-19-6, Diethyl (5-iodo-2-furanyl)phosphonate
 349110-34-5, N-(2,4-Difluorophenyl)-2-iodobenzamide 358672-63-6,
 N-(4-Chlorophenethyl)-2-iodobenzamide 358672-64-7, Methyl
 5-hydroxy-2-iodobenzoate 380430-56-8, 3-Amino-5-
 carbomethoxyphenylboronic acid 389057-75-4, 2-Amino-4-phosphonmethoxy-
 6,7,8,9-tetrahydronaphtho[1,2-d]thiazole 389057-78-7,
 4-Diphenylphosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole
 389057-79-8, 4-Phenylphosphonomethoxy-6,7,8,9-tetrahydronaphtho-[1,2-
 d]thiazole 389057-80-1, 4-Phosphonmethoxy-6,7,8,9-tetrahydronaphtho[1,2-
 d]thiazole

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant; combination of phosphonate or phosphorodiamidate FBPase
 inhibitors and antidiabetic agents useful for treatment of
 diabetes)

DOCUMENT NUMBER: 138:265470
 TITLE: Study of the insulinotropic effect of the novel
 antihyperglycemic agent KAD-1229 using HIT T15 cells,
 a hamster's insulinoma cell line
 AUTHOR(S): Ichikawa, Kiyoshi; Yamato, Tokuhisa; Tsuji, Atsutoshi;
 Ojima, Kazuma; Kusama, Hiroshi; Kojima, Masami
 CORPORATE SOURCE: Pharmacology Research, Research & Development, Kissei
 Pharmaceutical Co., Ltd., Hotaka, Nagano, Japan
 SOURCE: Arzneimittel-Forschung (2002), 52(8),
 605-609
 CODEN: ARZNAD; ISSN: 0004-4172
 PUBLISHER: Editio Cantor Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 02 Oct 2002
 AB The insulinotropic effect of (+)-monocalcium bis [(2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinyl-carbonyl)propionate]dihydrate (CAS 145375-43-5, KAD-1229) was assessed by comparing it with those of glibenclamide (CAS 10238-21-8), nateglinide (CAS 105816-04-4), and repaglinide (CAS 135062-02-1) using HIT T15 cells, a hamster insulinoma cell line. Although their potencies were different, KAD-1229, glibenclamide, nateglinide, and repaglinide all concentration-dependently and significantly induced insulin release from these cells. Further, each agent displaced the binding of ³H-glibenclamide to the cell membrane and inhibited ⁸⁶Rb⁺ efflux from the cells. These results indicate that KAD-1229, glibenclamide, nateglinide, and repaglinide each exert their insulinotropic effect by binding to the glibenclamide binding sites (sulfonylurea receptors) on pancreatic β -cells and closing K⁺ channels. Diazoxide, a K⁺ channel opener, and nitrendipine, a Ca²⁺ blocker, suppressed the insulin release induced by KAD-1229 or glibenclamide. These results demonstrate that the insulinotropic actions of KAD-1229 and glibenclamide involve similar underlying pathways.
 CC 1-10 (Pharmacology)
 ST antihyperglycemic KAD1229 insulinotrope pancreas beta cell
 diabetes mellitus; nateglinide repaglinide glibenclamide
 hypoglycemic KAD1229 diabetes; insulin secretagogue K channel
 calcium blocker sulfonylurea receptor antidiabetic
 IT Antidiabetic agents
 Diabetes mellitus
 (mechanism of antihyperglycemic agent KAD-1229 insulinotropic effect on
 hamster pancreatic β -cells)
 REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 23 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2001:635931 HCPLUS Full-text
 DOCUMENT NUMBER: 135:185506
 TITLE: Antidiabetic agents containing α -glucosidase
 inhibitors and insulin secretion promoters
 INVENTOR(S): Sugiyama, Yasuo; Odaka, Hiroyuki; Sakiyama, Hiroshi;
 Iwasaki, Masato; Funatsu, Masami
 PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
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| WO 2001062295 | A1 | 20010830 | WO 2001-JP1282 | 20010222 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2401356 | A1 | 20010830 | CA 2001-2401356 | 20010222 <-- |
| AU 2001034114 | A5 | 20010903 | AU 2001-34114 | 20010222 <-- |
| EP 1295609 | A1 | 20030326 | EP 2001-906193 | 20010222 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2001316293 | A | 20011113 | JP 2001-47695 | 20010223 <-- |
| US 2003040490 | A1 | 20030227 | US 2002-204783 | 20020821 <-- |
| PRIORITY APPLN. INFO.: | | | JP 2000-52297 | A 20000224 <-- |
| | | | WO 2001-JP1282 | W 20010222 <-- |

ED Entered STN: 31 Aug 2001

AB Drugs containing, as the active ingredients, exclusively a combination of an α -glucosidase inhibitor with a non-sulfonylurea insulin secretion promoter, are useful as preventives and remedies for diabetes, etc. Diabetic patients were administered with a tablet containing 0.2 mg voglibose and a tablet containing 2 mg repaglinide before breakfast and blood samples were taken 1 h after meals and the results showed a significant decrease in blood glucose levels.

IC ICM A61K045-06

ICS A61K031-44; A61K031-405; A61K031-198; A61K031-702; A61K031-133;
A61K031-70; A61P003-10; A61P043-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST antidiabetic glucosidase inhibitor insulin secretion promoter;
voglibose repaglinide diabetes control

IT Antidiabetic agents

(antidiabetic agents containing α -glucosidase inhibitors
and insulin secretion promoters)

IT Drug delivery systems

(tablets; antidiabetic agents containing α -glucosidase
inhibitors and insulin secretion promoters)

IT 56180-94-0, Acarbose 72432-03-2, Miglitol 80879-63-6, Emiglitate
83480-29-9, Voglibose 105816-04-4, Nateglinide 135062-02-1,
Repaglinide 145375-43-5, Mitiglinide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic agents containing α -glucosidase inhibitors
and insulin secretion promoters)

IT 9001-42-7, α -Glucosidase 9004-10-8, Insulin, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(antidiabetic agents containing α -glucosidase inhibitors
and insulin secretion promoters)

IT 50-99-7, D-Glucose, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(blood; antidiabetic agents containing α -glucosidase
inhibitors and insulin secretion promoters)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

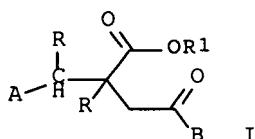
L61 ANSWER 24 OF 49 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:814308 HCPLUS Full-text
 DOCUMENT NUMBER: 133:359230
 TITLE: Use of succinic acid derivatives to obtain a medicine for treating inflammation
 INVENTOR(S): Caille, Dominique
 PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
 SOURCE: PCT Int. Appl., 13 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 2000067752 | A1 | 20001116 | WO 2000-FR1246 | 20000509 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| FR 2793411 | A1 | 20001117 | FR 1999-5978 | 19990511 <-- |
| FR 2793411 | B1 | 20010629 | | |
| EP 1178794 | A1 | 20020213 | EP 2000-927322 | 20000509 <-- |
| EP 1178794 | B1 | 20050907 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| JP 2002544163 | T | 20021224 | JP 2000-616778 | 20000509 <-- |
| AT 303807 | T | 20050915 | AT 2000-927322 | 20000509 <-- |
| PRIORITY APPLN. INFO.: | | | FR 1999-5978 | A 19990511 <-- |
| | | | WO 2000-FR1246 | W 20000509 <-- |

OTHER SOURCE(S): MARPAT 133:359230

ED Entered STN: 21 Nov 2000

GI



AB The invention concerns the use of succinic acid derivs. of general formula (I) wherein: A represents a Ph group optionally substituted by one, two or three substituents selected among a halogen, a C1-6 alkyl, C1-6 alkoxy group; a Ph, furyl, pyridyl or cycloalkyl with 3 to 8 carbon atoms; B represents an aminobicyclic group which consists of an amino cyclic compound with 5 or 6 members condensed with a cycloalkyl ring with 5 or 6 members which may have 1 or 2 unsatd. bonds, provided that B is bound to the carbon atom of the

carbonyl group on the nitrogen atom; each R represents a hydrogen atom and all the R radicals are combined together to form a chemical bond; R1 represents a hydrogen atom, a C1-6 alkyl group, an aralkyl group with 7 to 10 carbon atoms; when there exist geometric isomers, each geometric isomer, the isomers E and the isomers Z thereof, the isomers trans and the isomers cis, for treating inflammation. The compns. are administered at a daily dose of 1-100 mg orally, or 0.1-100 mg parenterally (no data).

IC ICM A61K031-4035
 ICS A61P029-00
 CC 1-7 (Pharmacology)
 ST succinic acid deriv inflammation inhibitor
 IT Nerve, disease
 (diabetic neuropathy; use of succinic acid derivs. to obtain medicine for treating inflammation)
 IT Arthritis
 (polyarthritis, inhibitors; use of succinic acid derivs. to obtain medicine for treating inflammation)
 IT 110-15-6D, Succinic acid, derivs. 145375-43-5
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (use of succinic acid derivs. to obtain medicine for treating inflammation)
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 161 25-49 ibib ab ind

L61 ANSWER 25 OF 49 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2005331235 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 15981944
 TITLE: Pharmacology of the meglitinide analogs: new treatment options for type 2 diabetes mellitus.
 AUTHOR: Malaisse Willy J
 CORPORATE SOURCE: Laboratory of Experimental Hormonology, Brussels Free University, Brussels, Belgium.. malaisse@ulb.ac.be
 SOURCE: Treatments in endocrinology, (2003) Vol. 2, No. 6, pp. 401-14. Ref: 83
 Journal code: 101132977. ISSN: 1175-6349.
 PUB. COUNTRY: New Zealand
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200507
 ENTRY DATE: Entered STN: 29 Jun 2005
 Last Updated on STN: 13 Jul 2005
 Entered Medline: 12 Jul 2005
 AB The expression meglitinide analogs was introduced in 1995 to cover new molecules proposed as non-sulfonylurea insulinotropic agents and displaying structural analogy with meglitinide, such as repaglinide, nateglinide, and mitiglinide. Meglitinide analogs display, as judged by conformation analysis, a U-shaped configuration similar to that of antihyperglycemic sulfonylureas such as glibenclamide (glyburide) and glimepiride. In rat pancreatic islets incubated in the presence of 7.0 mmol/L D-glucose, repaglinide and mitiglinide demonstrate comparable concentration-response relationships for stimulation of insulin release, with a threshold value < 10 nmol/L and a maximal secretory response at about 10 nmol/L. Several findings indicate that meglitinide analogs provoke the closing of adenosine triphosphate-sensitive potassium

channels, with subsequent gating of voltage-sensitive calcium channels. The effects of meglitinide analogs upon the binding of [³H]glibenclamide to islet cells membranes reinforces this concept. At variance, however, with other meglitinide analogs, the ionic and secretory response to repaglinide (10 micromol/L) is not rapidly reversible in perfused rat islets. In experiments conducted *in vivo* in control and diabetic rats, repaglinide provokes a greater and more rapid increase in plasma insulin concentration and an earlier fall in glycemia than glibenclamide or glimepiride. Onset of effect is also more rapid and duration of effect shorter with nateglinide versus glibenclamide. In clinical studies, single or repeated daily administration of repaglinide increased plasma insulin concentration in a dose-dependent manner, with an incremental peak reached about 2 hours after repaglinide intake. Plasma concentrations of repaglinide are about 5.0 microg/L 2-2.5 hours after oral intake of the drug. Despite the slow reversibility of repaglinide action *in vitro*, this drug offers advantages over glibenclamide in terms of the possible occurrence of hypoglycemia if a meal is missed. In volunteers receiving a single oral dose of nateglinide (120mg) 10 minutes before a standardized 800 Kcal breakfast, the plasma insulin concentration was higher 5, 10, and 20 minutes after meal intake than when they received a single dose of repaglinide (0.5 or 2.0mg) or placebo 10 minutes before breakfast. Peak plasma concentrations of nateglinide were reached within 2 hours in most volunteers. Peak plasma concentrations of mitiglinide were reached 30 minutes after a single oral dose in a representative volunteer. Mitiglinide significantly suppressed meal-induced elevations in blood glucose concentrations in a study of patients with type 2 diabetes. In conclusion, two obvious differences among these meglitinide analogs should be underlined. First, on a molar basis, nateglinide is somewhat less potent than repaglinide or mitiglinide, as an insulinotropic agent. The maximal secretory responses evoked by these three meglitinide analogs are, however, identical to one another. Secondly, and as already mentioned, the functional effects of nateglinide and mitiglinide are more rapidly reversible than those of repaglinide, for instance in perfused rat islets. The meglitinide analogs offer the advantage over the long-acting antihyperglycemic sulfonylurea glibenclamide of minimizing the risk of undesirable hypoglycemia.

CT

Animals

- *Benzamides: TU, therapeutic use
- *Carbamates: TU, therapeutic use
- *Cyclohexanes: TU, therapeutic use
 - *Diabetes Mellitus, Type 2: DT, drug therapy

Humans

- *Hypoglycemic Agents: TU, therapeutic use
- *Phenylalanine: AA, analogs & derivatives
- *Phenylalanine: TU, therapeutic use
- *Piperidines: TU, therapeutic use

RN

105816-04-4 (nateglinide); 135062-02-1 (repaglinide); 54870-28-9
(meglitinide); 63-91-2 (Phenylalanine)

CN

0 (Benzamides); 0 (Carbamates); 0 (Cyclohexanes); 0 (Hypoglycemic Agents);
0 (Piperidines)

L61 ANSWER 26 OF 49 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2002271275 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12010187

TITLE: Effect of KAD-1229, a novel hypoglycaemic agent, on plasma glucose levels after meal load in type 2 diabetic rats.

AUTHOR: Ichikawa Kiyoshi; Yamato Tokuhisa; Ojima Kazuma; Tsuji Atsutoshi; Ishikawa Kohtaro; Kusama Hiroshi; Kojima Masami

CORPORATE SOURCE: Pharmacology Laboratories, Kissei Pharmaceutical Co. Ltd, Hotaka, Nagano, Japan.. kiyoshi_ichikawa@pharm.kissei.co.jp

SOURCE: Clinical and experimental pharmacology & physiology,

(2002 May-Jun) Vol. 29, No. 5-6, pp. 423-7.
 Journal code: 0425076. ISSN: 0305-1870.

PUB. COUNTRY: Australia
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200208
 ENTRY DATE: Entered STN: 16 May 2002
 Last Updated on STN: 30 Aug 2002
 Entered Medline: 29 Aug 2002

AB 1. The effects of KAD-1229 (a novel non-sulphonylurea agent), voglibose (an alpha-glucosidase inhibitor) and nateglinide (a non-sulphonylurea antihyperglycaemic agent) on hyperglycaemia induced by a meal load were assessed in diabetic rats. 2. KAD-1229 suppressed the increase in plasma glucose levels seen after a meal load and the area under the curve for plasma glucose levels (AUCglucose) up to 5 h after the meal load. 3. Voglibose also suppressed the increase in plasma glucose levels; however, a significant decrease in AUCglucose following voglibose was not observed. 4. Nateglinide suppressed the increase in plasma glucose levels at 30 min and 1 h after the meal load; however, plasma glucose levels was above control thereafter and the AUCglucose was not decreased. 5. The results indicate that KAD-1229 has an antihyperglycaemic effect and KAD-1229 is suggested to be a suitable agent for controlling post-prandial hyperglycaemia.

CT Animals
 *Blood Glucose: ME, metabolism
 Cyclohexanes: PD, pharmacology
 Diabetes Mellitus, Experimental: BL, blood
 *Diabetes Mellitus, Experimental: DT, drug therapy
 Diabetes Mellitus, Type 2: BL, blood
 *Diabetes Mellitus, Type 2: DT, drug therapy

Food
 *Hypoglycemic Agents: PD, pharmacology
 *Indoles: PD, pharmacology
 *Inositol: AA, analogs & derivatives
 Inositol: PD, pharmacology
 *Phenylalanine: AA, analogs & derivatives
 Phenylalanine: PD, pharmacology
 *Postprandial Period

Rats
 Rats, Wistar
 Species Specificity

RN 105816-04-4 (nateglinide); 63-91-2 (Phenylalanine); 6917-35-7 (Inositol);
 83480-29-9 (voglibose)

CN 0 (Blood Glucose); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles);
 0 (mitiglinide)

L61 ANSWER 27 OF 49 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 2001260288 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 11264248
 TITLE: Effects of mitiglinide (S 21403) on Kir6.2/SUR1,
 Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive
 potassium channel.
 AUTHOR: Reimann F; Proks P; Ashcroft F M
 CORPORATE SOURCE: University Laboratory of Physiology, Parks Road, Oxford OX1
 3PT.
 SOURCE: British journal of pharmacology, (2001 Apr) Vol.
 132, No. 7, pp. 1542-8.
 Journal code: 7502536. ISSN: 0007-1188.
 PUB. COUNTRY: England: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200105
 ENTRY DATE: Entered STN: 21 May 2001
 Last Updated on STN: 21 May 2001
 Entered Medline: 17 May 2001

AB 1. We have investigated the mechanism of action of the novel anti-diabetic agent mitiglinide (S 21403) on Kir6.2/SUR1, Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive potassium (K(ATP)) channel. These possess a common pore-forming subunit, Kir6.2, and different regulatory sulphonylurea receptor (SUR) subunits. It is believed that they correspond to native K(ATP) channels in pancreatic beta-cells, heart and non-vascular smooth muscle, respectively. 2. Kir6.2 was coexpressed with SUR1, SUR2A or SUR2B in Xenopus oocytes and macroscopic currents were recorded in giant inside-out membrane patches. Mitiglinide was added to the intracellular membrane surface. 3. Mitiglinide inhibited Kir6.2/SUR currents at two sites: a low-affinity site on Kir6.2 and a high-affinity site on SUR. Low-affinity inhibition was similar for all three types of K(ATP) channel but high-affinity inhibition was greater for Kir6.2/SUR1 currents (IC_{50} , 4 nM) than for Kir6.2/SUR2A or Kir6.2/SUR2B currents (IC_{50} , 3 and 5 microM, respectively). 4. Inhibition of Kir6.2/SUR1 currents was only slowly reversible on the time scale of electrophysiological experiments. 5. Kir6.2/SUR1-S1237Y currents, which previously have been shown to lack high affinity tolbutamide inhibition, resembled Kir6.2/SUR2 currents in being unaffected by 100 nM but blocked by 10 microM mitiglinide. 6. Our results show that mitiglinide is a high-affinity drug that shows a 1000 fold greater affinity for the beta-cell type than the cardiac and smooth muscle types of K(ATP) channel, when measured in excised patches.

CT Check Tags: Female
 *Adenosine Triphosphate: PH, physiology
 Animals
 Dose-Response Relationship, Drug
 *Indoles: PD, pharmacology
 Membrane Potentials: DE, drug effects
 Mice
 *Potassium Channels: DE, drug effects
 Potassium Channels: GE, genetics
 Potassium Channels: PH, physiology
 *Potassium Channels, Inwardly Rectifying
 Protein Subunits
 RNA, Messenger: AD, administration & dosage
 RNA, Messenger: GE, genetics
 Xenopus laevis

RN 56-65-5 (Adenosine Triphosphate)
 CN 0 (Indoles); 0 (Potassium Channels); 0 (Potassium Channels, Inwardly Rectifying); 0 (Protein Subunits); 0 (RNA, Messenger); 0 (mitiglinide)

L61 ANSWER 28 OF 49 MEDLINE on STN DUPLICATE 5
 ACCESSION NUMBER: 2001689244 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 11716850
 TITLE: The effects of mitiglinide (KAD-1229), a new anti-diabetic drug, on ATP-sensitive K⁺ channels and insulin secretion: comparison with the sulfonylureas and nateglinide.
 AUTHOR: Sunaga Y; Gono T; Shibasaki T; Ichikawa K; Kusama H; Yano H; Seino S
 CORPORATE SOURCE: Department of Cellular and Molecular Medicine, Graduate School of Medicine, Chiba University 1-8-1 Inohana, Chuo-ku, 260-8670, Chiba, Japan.

SOURCE: European journal of pharmacology, (2001 Nov 9)
 Vol. 431, No. 1, pp. 119-25.
 Journal code: 1254354. ISSN: 0014-2999.

PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: (COMPARATIVE STUDY)
 Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200201
 ENTRY DATE: Entered STN: 11 Dec 2001
 Last Updated on STN: 25 Jan 2002
 Entered Medline: 11 Jan 2002

AB Mitiglinide (KAD-1229), a new anti-diabetic drug, is thought to stimulate insulin secretion by closing the ATP-sensitive K⁺ (K(ATP)) channels in pancreatic beta-cells. However, its selectivity for the various K(ATP) channels is not known. In this study, we examined the effects of mitiglinide on various cloned K(ATP) channels (Kir6.2/SUR1, Kir6.2/SUR2A, and Kir6.2/SUR2B) reconstituted in COS-1 cells, and compared them to another meglitinide-related compound, nateglinide. Patch-clamp analysis using inside-out recording configuration showed that mitiglinide inhibits the Kir6.2/SUR1 channel currents in a dose-dependent manner (IC₅₀ value, 100 nM) but does not significantly inhibit either Kir6.2/SUR2A or Kir6.2/SUR2B channel currents even at high doses (more than 10 microM). Nateglinide inhibits Kir6.2/SUR1 and Kir6.2/SUR2B channels at 100 nM, and inhibits Kir6.2/SUR2A channels at high concentrations (1 microM). Binding experiments on mitiglinide, nateglinide, and repaglinide to SUR1 expressed in COS-1 cells revealed that they inhibit the binding of [³H]glibenclamide to SUR1 (IC₅₀ values: mitiglinide, 280 nM; nateglinide, 8 microM; repaglinide, 1.6 microM), suggesting that they all share a glibenclamide binding site. The insulin responses to glucose, mitiglinide, tolbutamide, and glibenclamide in MIN6 cells after chronic mitiglinide, nateglinide, or repaglinide treatment were comparable to those after chronic tolbutamide and glibenclamide treatment. These results indicate that, similar to the sulfonylureas, mitiglinide is highly specific to the Kir6.2/SUR1 complex, i.e., the pancreatic beta-cell K(ATP) channel, and suggest that mitiglinide may be a clinically useful anti-diabetic drug.

CT *ATP-Binding Cassette Transporters

- Animals
- COS Cells
- Cell Line
- Cyclohexanes: PD, pharmacology
- Glyburide: PD, pharmacology
- *Hypoglycemic Agents: PD, pharmacology
- *Indoles: PD, pharmacology
- *Insulin: ME, metabolism
- Patch-Clamp Techniques
- *Phenylalanine: AA, analogs & derivatives
- Phenylalanine: PD, pharmacology
- Potassium Channels: GE, genetics
- *Potassium Channels: ME, metabolism
- *Potassium Channels, Inwardly Rectifying
- Receptors, Drug: GE, genetics
- Receptors, Drug: ME, metabolism
- Sulfonylurea Compounds: PD, pharmacology
- Tolbutamide: PD, pharmacology
- Transfection

RN 10238-21-8 (Glyburide); 105816-04-4 (nateglinide); 11061-68-0 (Insulin);
 63-91-2 (Phenylalanine); 64-77-7 (Tolbutamide)

CN 0 (ATP-Binding Cassette Transporters); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Potassium Channels); 0 (Potassium Channels,

Inwardly Rectifying); 0 (Receptors, Drug); 0 (Sulfonylurea Compounds); 0 (mitiglinide); 0 (sulfonylurea receptor)

L61 ANSWER 29 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 2006653767 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 17087304
 TITLE: Glinide(s), sulfonylurea(s).
 AUTHOR: Arakawa Masayuki; Hirose Takahisa
 CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology,
 Juntendo University School of Medicine.
 SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2006
 Nov) Vol. 64, No. 11, pp. 2107-12. Ref: 16
 Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan
 DOCUMENT TYPE: (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200701

ENTRY DATE: Entered STN: 8 Nov 2006
 Last Updated on STN: 10 Jan 2007
 Entered Medline: 9 Jan 2007

AB Diabetic macroangiopathy has already developed before diagnosis of diabetes mellitus. Postprandial hyperglycemia has been known as a risk factor for diabetic macroangiopathy and may be more powerful than fasting hyperglycemia. To intervene in hyperglycemia, insulin secretagogues, glinides which selectively stimulate early meal-induced insulin secretion and improve postprandial hyperglycemia, and sulfonylureas which enhance total daily insulin secretion and improve fasting hyperglycemia, have been prescribed as major oral antidiabetic agents. Few evidences that amelioration of glycemic control with insulin secretagogues lower the risk of cardiovascular diseases have been reported. But current studies have shown that intervention in postprandial hyperglycemia with drugs including glinides decreased thickness of carotid IMT as a surrogate marker of atherosclerosis. Results from on-going large scale intervention study with glinides may clarify whether amelioration of hyperglycemia lower the risk of atherosclerotic events.

CT Arteriosclerosis: ET, etiology
 *Arteriosclerosis: PC, prevention & control
 Cardiovascular Diseases: ET, etiology
 *Cardiovascular Diseases: PC, prevention & control
 *Cyclohexanes: TU, therapeutic use
 Diabetic Angiopathies: ET, etiology
 *Diabetic Angiopathies: PC, prevention & control
 Glucose Intolerance: CO, complications
 Glucose Intolerance: DT, drug therapy
 Hyperglycemia: CO, complications
 *Hyperglycemia: DT, drug therapy
 Hyperglycemia: PP, physiopathology
 *Hypoglycemic Agents: TU, therapeutic use
 *Indoles: TU, therapeutic use
 Insulin: SE, secretion
 *Phenylalanine: AA, analogs & derivatives
 Phenylalanine: TU, therapeutic use
 Postprandial Period
 Risk Factors
 *Sulfonylurea Compounds: TU, therapeutic use
 RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine)
 CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Sulfonylurea Compounds); 0 (mitiglinide)

L61 ANSWER 30 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 2005676318 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 16363700
 TITLE: Significance of insulin secretion pattern lectured by "glinides" in the treatment of postprandial hyperglycemia.
 AUTHOR: Hirose Takahisa
 CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology, Juntendo University School of Medicine.
 SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005 Dec) Vol. 63, No. 12, pp. 2237-44. Ref: 14
 Journal code: 0420546. ISSN: 0047-1852.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: Japanese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200603
 ENTRY DATE: Entered STN: 22 Dec 2005
 Last Updated on STN: 11 Mar 2006
 Entered Medline: 10 Mar 2006

AB The mechanisms by which postprandial hyperglycemia is elicited were discussed through therapies of type 2 diabetes using "glinides". It has been believed that the earliest determinant of progression to type 2 diabetes is a loss of early insulin secretion, a defect which results in postprandial hyperglycemia and is often believed to reflect insulin resistance. To prove that, we improved insulin secretion pattern without increase of total amount of insulin secretion using glinide and assessed glucose response. Glinide which selectively enhances early meal-induced insulin secretion improved postprandial hyperglycemia, could provide a valuable treatment option in the prevention and treatment of type 2 diabetes.

CT *Cyclohexanes: TU, therapeutic use
 Diabetes Mellitus, Type 2: CO, complications

Eating

Humans

*Hyperglycemia: DT, drug therapy

Hyperglycemia: ET, etiology

*Hypoglycemic Agents: TU, therapeutic use

*Indoles: TU, therapeutic use

*Insulin: SE, secretion

*Phenylalanine: AA, analogs & derivatives

Phenylalanine: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine)

CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 31 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 2005147537 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 15779420
 TITLE: Effects of mitiglinide in treatment of impaired glucose tolerance.
 AUTHOR: Katahira Hiroshi; Ishida Hitoshi
 CORPORATE SOURCE: Third Department of Internal Medicine, Kyorin University School of Medicine.
 SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005 Feb) Vol. 63 Suppl 2, pp. 444-50. Ref: 15
 Journal code: 0420546. ISSN: 0047-1852.
 PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: Japanese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200506
 ENTRY DATE: Entered STN: 23 Mar 2005
 Last Updated on STN: 15 Jun 2005
 Entered Medline: 14 Jun 2005
 CT Adenosine Triphosphate: ME, metabolism
 Animals
 Diabetes Mellitus, Type 2: ET, etiology
 Diabetes Mellitus, Type 2: PC, prevention & control
 Humans
 Hyperglycemia: CO, complications
 *Hyperglycemia: DT, drug therapy
 Hypoglycemic Agents: PK, pharmacokinetics
 *Hypoglycemic Agents: PD, pharmacology
 *Hypoglycemic Agents: TU, therapeutic use
 Indoles: PK, pharmacokinetics
 *Indoles: PD, pharmacology
 *Indoles: TU, therapeutic use
 *Insulin: SE, secretion
 Postprandial Period
 Potassium Channels: DE, drug effects
 Stimulation, Chemical
 RN 11061-68-0 (Insulin); 56-65-5 (Adenosine Triphosphate)
 CN 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Potassium Channels); 0 (mitiglinide)

L61 ANSWER 32 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 2005147534 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 15779417
 TITLE: Selection of oral antidiabetic drugs.
 AUTHOR: Iwamoto Yasuhiko
 CORPORATE SOURCE: Diabetes Center, Tokyo Women's Medical University.
 SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005
 Feb) Vol. 63 Suppl 2, pp. 428-32. Ref: 9
 Journal code: 0420546. ISSN: 0047-1852.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: Japanese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200506
 ENTRY DATE: Entered STN: 23 Mar 2005
 Last Updated on STN: 15 Jun 2005
 Entered Medline: 14 Jun 2005
 CT Acarbose
 Administration, Oral
 Biguanides
 Cardiovascular Diseases: ET, etiology
 Cardiovascular Diseases: PC, prevention & control
 Diabetes Mellitus, Type 2: ET, etiology
 Diabetes Mellitus, Type 2: PC, prevention & control
 Enzyme Inhibitors
 Glucose Intolerance: CO, complications
 Glucose Intolerance: DT, drug therapy
 Humans
 *Hypoglycemic Agents
 Hypoglycemic Agents: AD, administration & dosage

Hypoglycemic Agents: AE, adverse effects

Hypoglycemic Agents: CL, classification

Hypoglycemic Agents: PD, pharmacology

Indoles

Risk

Sulfonylurea Compounds

Thiazolidinediones

alpha-Glucosidases: AI, antagonists & inhibitors

RN 2295-31-0 (2,4-thiazolidinedione); 56180-94-0 (Acarbose)

CN 0 (Biguanides); 0 (Enzyme Inhibitors); 0 (Hypoglycemic Agents);

0 (Indoles); 0 (Sulfonylurea Compounds); 0 (Thiazolidinediones); 0 (mitiglinide); EC 3.2.1.20 (alpha-Glucosidases)

L61 ANSWER 33 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2004624721 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 15561904

TITLE: The impact of ATP-sensitive K⁺ channel subtype selectivity of insulin secretagogues for the coronary vasculature and the myocardium.

AUTHOR: Quast Ulrich; Stephan Damian; Bieger Susanne; Russ Ulrich

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical Faculty, University of Tubingen, Wilhelmstrasse. 56, D-72074 Tubingen, Germany.. ulrich.quast@uni-tuebingen.de

SOURCE: Diabetes, (2004 Dec) Vol. 53 Suppl 3, pp. S156-64. Ref: 58 Journal code: 0372763. ISSN: 0012-1797.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200504

ENTRY DATE: Entered STN: 20 Dec 2004

Last Updated on STN: 15 Apr 2005

Entered Medline: 14 Apr 2005

AB Insulin secretagogues (sulfonylureas and glinides) increase insulin secretion by closing the ATP-sensitive K⁺ channel (KATP channel) in the pancreatic beta-cell membrane. KATP channels subserve important functions also in the heart. First, KATP channels in coronary myocytes contribute to the control of coronary blood flow at rest and in hypoxia. Second, KATP channels in the sarcolemma of cardiomyocytes (sarckATP channels) are required for adaptation of the heart to stress. In addition, the opening of sarckATP channels and of KATP channels in the inner membrane of mitochondria (mitoKATP channels) plays a central role in ischemic preconditioning. Opening of sarckATP channels also underlies the ST-segment elevation of the electrocardiogram, the primary diagnostic tool for initiation of lysis therapy in acute myocardial infarction. Therefore, inhibition of cardiovascular KATP channels by insulin secretagogues is considered to increase cardiovascular risk.

Electrophysiological experiments have shown that the secretagogues differ in their selectivity for the pancreatic over the cardiovascular KATP channels, being either highly selective (approximately 1,000x; short sulfonylureas such as nateglinide and mitiglinide), moderately selective (10-20x; long sulfonylureas such as glibenclamide [glyburide]), or essentially nonselective (<2x; repaglinide). New binding studies presented here give broadly similar results. In clinical studies, these differences are not yet taken into account. The hypothesis that the in vitro selectivity of the insulin secretagogues is of importance for the cardiovascular outcome of diabetic patients with coronary artery disease needs to be tested.

CT *Adenosine Triphosphate: PH, physiology
Animals

*Coronary Circulation: PH, physiology
 *Heart: PH, physiology
 Humans
 *Hypoglycemic Agents: PD, pharmacology
 *Insulin: SE, secretion
 Models, Molecular
 Potassium Channels, Inwardly Rectifying: CH, chemistry
 Potassium Channels, Inwardly Rectifying: DE, drug effects
 *Potassium Channels, Inwardly Rectifying: PH, physiology
 Protein Conformation
 Protein Subunits: CH, chemistry
 Sulfonylurea Compounds: PD, pharmacology

RN 11061-68-0 (Insulin); 56-65-5 (Adenosine Triphosphate)
 CN 0 (Hypoglycemic Agents); 0 (Kir6.2 channel); 0 (Potassium Channels, Inwardly Rectifying); 0 (Protein Subunits); 0 (Sulfonylurea Compounds)

L61 ANSWER 34 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 2004390172 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 15293870
 TITLE: Mitiglinide: KAD 1229, S 21403.
 AUTHOR: Anonymous
 SOURCE: Drugs in R&D, (2004) Vol. 5, No. 2, pp. 98-101. Ref: 13
 Journal code: 100883647. ISSN: 1174-5886.
 PUB. COUNTRY: New Zealand
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200502
 ENTRY DATE: Entered STN: 6 Aug 2004
 Last Updated on STN: 4 Feb 2005
 Entered Medline: 3 Feb 2005

AB Mitiglinide [KAD 1229, S 21403], a derivative of benzylsuccinic acid, is a potassium channel antagonist undergoing development with Kissei for the treatment of type 2 diabetes mellitus. It has potent oral hypoglycaemic activity and is structurally different from the sulphonylureas, although it stimulates calcium influx by binding to the suphonylurea receptor on pancreatic beta-cells and closing K⁺ATP channels. Mitiglinide belongs to a family of meglitinide analogues that also includes repaglinide and nateglinide. Mitiglinide is licensed to Servier for Europe, where it is undergoing phase III development, and for Russia, the Commonwealth of Independent States, the Baltic Republics, the Middle East, Oceania, China (including Hong Kong) and Taiwan. Kissei exclusively licensed mitiglinide to Choongwae Pharma for South Korea in March 2003. In August 2002, Kissei and Takeda entered into a co-marketing agreement for mitiglinide in Japan. The companies will co-market the agent under a single brand name. Mitiglinide was licensed to Purdue Pharma for the US, Canada, Mexico and Central and South America. However, Kissei and Purdue Pharma terminated their agreement in February 2001 following Purdue Pharma's decision to concentrate on core areas such as oncology and analgesics. Kissei's US subsidiary, Kissei Pharma US, is currently carrying on the ongoing phase II clinical development in the US. However, in its Annual Report 2003, Kissei announced that it is considering outlicensing mitiglinide for development in marketing in North America. Mitiglinide has been recommended for approval in Japan for the management of postprandial hyperglycaemia in patients with type 2 diabetes. Kissei is also conducting phase II/III clinical trials with a combination of mitiglinide and an alpha-glucosidase inhibitor (additional indication) in patients with type 2 diabetes in Japan. In the US, the agent is being evaluated in phase II clinical trials with Kissei Pharma USA. Mitiglinide is also undergoing a phase-III, 12-month, multicentre, randomised, double-blind study in a total of

710 patients in comparison with repaglinide for the treatment of type 2 diabetes. This study will be followed by a 12-month open-label treatment with mitiglinide alone or in combination therapy. Servier (Australia) conducted a randomised, double-blind, multicentre phase III study in Australia comparing mitiglinide with metformin or a combination of the two for the treatment of type 2 diabetes.

CT Animals

Diabetes Mellitus, Type 2: DT, drug therapy

Humans

Hypoglycemic Agents: PD, pharmacology

*Hypoglycemic Agents: TU, therapeutic use

Indoles: PD, pharmacology

*Indoles: TU, therapeutic use

Randomized Controlled Trials

CN 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 35 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2003345780 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12877090

TITLE: Nateglinide and mitiglinide.

AUTHOR: Odawara Masato

CORPORATE SOURCE: Department of Endocrinology and Metabolism, Toranomon Hospital.

SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2003 Jul) Vol. 61, No. 7, pp. 1230-7. Ref: 12 Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)

Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200309

ENTRY DATE: Entered STN: 25 Jul 2003

Last Updated on STN: 26 Sep 2003

Entered Medline: 25 Sep 2003

AB Patients with type 2 diabetes mellitus are associated with insulin resistance and/or impaired insulin secretion. Previous observations indicate that Japanese patients with type 2 diabetes tend to have impaired insulin response after glycemic load more often than Caucasian counterparts. Recently it has been reported that hyperglycemia after glucose load is itself a risk factor for the development of cardiovascular complications in the absence of elevated fasting plasma glucose. Recent observations on the association of post-challenge or post-prandial hyperglycemia with cardiovascular events suggest that lowering post-prandial plasma glucose may protect patients from developing cardiovascular diseases. Results of STOP-NIDDM trial suggest that nateglinide, which attenuates post-prandial glycemic surge in type 2 diabetes, may also be helpful for the protection against cardiovascular events. Nateglinide exerts its effects shortly after its administration and the effects continue for only about 3 hours. The patients receiving this agent rarely gain weight and develop hypoglycemia. This agent exerts hypoglycemic effects additively with alpha-gulcosidase inhibitors or metformin.

CT Cardiovascular Diseases: ET, etiology

Cardiovascular Diseases: PC, prevention & control

Cyclohexanes: PD, pharmacology

*Cyclohexanes: TU, therapeutic use

Diabetes Mellitus, Type 2: CO, complications

Diabetes Mellitus, Type 2: DT, drug therapy

Drug Therapy, Combination

Humans

Hyperglycemia: CO, complications
 *Hyperglycemia: DT, drug therapy
 *Hypoglycemic Agents: TU, therapeutic use
 Indoles: PD, pharmacology
 *Indoles: TU, therapeutic use
 *Insulin: SE, secretion
 Insulin Resistance
 Metformin: TU, therapeutic use
 Phenylalanine: AA, analogs & derivatives
 Phenylalanine: PD, pharmacology
 *Phenylalanine: TU, therapeutic use
 Postprandial Period
 Stimulation, Chemical
 RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine);
 657-24-9 (Metformin)
 CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 36 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2002028119 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 11472274
 TITLE: Rapid acting insulinotropic agents: restoration of early insulin secretion as a physiologic approach to improve glucose control.
 AUTHOR: Pratley R E; Foley J E; Dunning B E
 CORPORATE SOURCE: Novartis Pharmaceuticals Corporation, 59 Route 10, East Hanover, New Jersey 07936, USA..
 richard.pratley@pharma.novartis.com
 SOURCE: Current pharmaceutical design, (2001 Sep) Vol. 7, No. 14, pp. 1375-97. Ref: 143
 Journal code: 9602487. ISSN: 1381-6128.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200112
 ENTRY DATE: Entered STN: 21 Jan 2002
 Last Updated on STN: 21 Jan 2002
 Entered Medline: 4 Dec 2001
 AB The loss of early insulin secretion appears to be a critical event in the deterioration in glucose tolerance during the development of type 2 diabetes. There is therefore a strong rationale for developing new antidiabetic agents aimed at restoring or replacing early prandial insulin secretion and thereby curbing mealtime glucose excursions in patients with type 2 diabetes. Four such new agents are either now available (repaglinide and nateglinide) or in clinical development (KAD-1229 and BTS 67 582). Preclinical studies suggest that each of these new insulinotropic agents share a common receptor/effect mechanism with the sulfonylureas (SUs) but that each may have distinct characteristics that differentiate them from the SUs and from each other. Nateglinide and KAD-1229 clearly stimulate biphasic insulin secretion in vitro and in vivo and their effects are rapidly reversible, whereas the effects of repaglinide and BTS 67 582 are prolonged well beyond their removal from perfusion media in vitro or their clearance in vivo. Available data from human studies indicate that the pharmacokinetics of repaglinide and nateglinide are similar, i.e., they are both rapidly absorbed and eliminated, but consistent with findings from animal studies, the insulinotropic and glucose-lowering effects of repaglinide are slower in onset and more prolonged than those of nateglinide. Repaglinide and nateglinide have been shown to be safe and well-tolerated in patients with type 2 diabetes and to produce

10/519155

clinically-meaningful reductions of HbA1c, both alone and in combination with agents with complementary modes of action (e.g., metformin and thiazolidinediones). Because these new agents can potentially bring patients to near normoglycemia without an undue risk of hypoglycemia, they are important additions to the therapeutic armamentarium.

CT Animals

Carbamates: CH, chemistry

Carbamates: PK, pharmacokinetics

Carbamates: TU, therapeutic use

Cyclohexanes: CH, chemistry

Cyclohexanes: PK, pharmacokinetics

Cyclohexanes: TU, therapeutic use

*Diabetes Mellitus, Type 2: BL, blood

*Diabetes Mellitus, Type 2: DT, drug therapy

*Glucose: ME, metabolism

Guanidines: CH, chemistry

Guanidines: PK, pharmacokinetics

Guanidines: TU, therapeutic use

Humans

Hypoglycemic Agents: CH, chemistry

Hypoglycemic Agents: PK, pharmacokinetics

*Hypoglycemic Agents: TU, therapeutic use

Indoles: CH, chemistry

Indoles: PK, pharmacokinetics

Indoles: TU, therapeutic use

Insulin: BL, blood

Insulin: PH, physiology

*Insulin: SE, secretion

*Phenylalanine: AA, analogs & derivatives

Phenylalanine: CH, chemistry

Phenylalanine: PK, pharmacokinetics

Phenylalanine: TU, therapeutic use

Piperidines: CH, chemistry

Piperidines: PK, pharmacokinetics

Piperidines: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 135062-02-1

(repaglinide); 50-99-7 (Glucose); 63-91-2 (Phenylalanine)

CN 0 (BTS 67582); 0 (Carbamates); 0 (Cyclohexanes); 0 (Guanidines); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Piperidines); 0 (mitiglinide)

L61 ANSWER 37 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2001301378 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11174074

TITLE: Effect of KAD-1229, a nonsulfonylurea hypoglycemic agent, on plasma glucose and insulin in streptozotocin-induced diabetic dogs.

AUTHOR: Misawa K; Ichikawa K; Ojima K; Hamano S; Kitamura T; Komatsu H

CORPORATE SOURCE: Pharmacological Laboratories, Kissei Pharmaceutical Co. Ltd., Hotaka, Nagano, Japan.. keiko_misawa@pharm.kissei.co.jp

SOURCE: Pharmacology, (2001 Feb) Vol. 62, No. 2, pp. 65-72.

Journal code: 0152016. ISSN: 0031-7012.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200105

ENTRY DATE: Entered STN: 4 Jun 2001
 Last Updated on STN: 4 Jun 2001
 Entered Medline: 31 May 2001

AB Hypoglycemic agents with a rapid onset and short duration of action should be useful for controlling postprandial hyperglycemia. Our aim was to establish a diabetes mellitus model in dogs, and then during an oral glucose tolerance test to compare the hypoglycemic effect and insulinotropic action of KAD-1229, a new hypoglycemic agent, with that of gliclazide, a conventional sulfonylurea. In this model, KAD-1229 reduced the increase in plasma glucose level without producing hypoglycemia. Gliclazide had a weaker effect on reduction of the glucose increase and caused hypoglycemia via a significantly raised insulin secretion in the late phase. A rapid insulinotropic action of KAD-1229 was clearly observed in the portal venous blood. The results suggest that in type 2 diabetes caused by, at least, insulin deficiency, KAD-1229 may improve impaired insulin secretion in the early phase and attenuate hyperglycemia without causing a sustained hypoglycemia. Copyright 2001 S. Karger AG, Basel.

CT Check Tags: Male
 Animals
 Anti-Bacterial Agents
 *Blood Glucose: DE, drug effects
 *Diabetes Mellitus, Experimental: BL, blood
 Disease Models, Animal
 Dogs
 Gliclazide: PD, pharmacology
 Glucose Tolerance Test
 *Hypoglycemic Agents: PD, pharmacology
 *Indoles: PD, pharmacology
 *Insulin: BL, blood
 Streptozocin

RN 11061-68-0 (Insulin); 18883-66-4 (Streptozocin); 21187-98-4 (Gliclazide)
 CN 0 (Anti-Bacterial Agents); 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 38 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 1999215370 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 10199157
 TITLE: Non-SU, insulin secretagogues.
 AUTHOR: Kikuchi M
 CORPORATE SOURCE: Institute for Adult Diseases, Asahi Life Foundation.
 SOURCE: Nippon rinsho. Japanese journal of clinical medicine,
 (1999 Mar) Vol. 57, No. 3, pp. 702-8. Ref: 21
 Journal code: 0420546. ISSN: 0047-1852.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: Japanese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199905
 ENTRY DATE: Entered STN: 1 Jun 1999
 Last Updated on STN: 1 Jun 1999
 Entered Medline: 18 May 1999

AB The chemical structures, mechanisms of actions, bioavailabilities, insulinotropic and hypoglycemic actions, and clinical trials of three novel oral hypoglycemic agents, NN-623, A-4166 and KAD-1229 are overviewed. They are non-SU insulin secretagogues and they induce quicker and shorter hypoglycemia than sulphonylureas do, presumably because they are rapidly absorbed into (Tmax: < 30 min) and excreted from blood (T 1/2: < 60 min). They bind to the SU-receptors and suppress K-ATP channels like sulphonylureas

do. They stimulate mainly the initial phase of insulin release and evoke a decrease in postprandial rises in plasma glucose in several animals and humans. Clinical trials demonstrated they are efficacious and safe in the treatment of NIDDM subjects. They are useful as a first choice drug for the early stage of NIDDM.

CT *Cyclohexanes: TU, therapeutic use
 *Diabetes Mellitus, Type 2: DT, drug therapy

Humans

*Hypoglycemic Agents: TU, therapeutic use

*Indoles: TU, therapeutic use

*Phenylalanine: AA, analogs & derivatives

Phenylalanine: TU, therapeutic use

RN 105816-04-4 (nateglinide); 63-91-2 (Phenylalanine)

CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 39 OF 49 MEDLINE on STN

ACCESSION NUMBER: 1999410611 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10479476

TITLE: Effect of the meglitinide analog S21403 on cationic fluxes and insulin release in perfused rat pancreatic islets exposed to a high concentration of D-glucose.

AUTHOR: Louchami K; Jijakli H; Malaisse W J

CORPORATE SOURCE: Laboratory of Experimental Medicine, Brussels Free University, 808 Route de Lennik, Brussels, B-1070, Belgium.

SOURCE: Pharmacological research : the official journal of the Italian Pharmacological Society, (1999 Sep) Vol. 40, No. 3, pp. 297-300.

Journal code: 8907422. ISSN: 1043-6618.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199911

ENTRY DATE: Entered STN: 11 Jan 2000

Last Updated on STN: 11 Jan 2000

Entered Medline: 1 Nov 1999

AB The effect of the meglitinide analog S21403 (10 microm) upon (86)Rb and (45)Ca outflow and insulin release was investigated in perfused rat islets exposed to a high concentration of D-glucose (16.7 mm) in order to simulate the situation found in diabetic patients. Under these conditions, S21403 provoked a rapid, sustained and rapidly reversible increase in (86)Rb outflow, (45)Ca efflux and insulin release. These effects were suppressed or reversed when the experiments were conducted in the absence of extracellular Ca²⁺. They support the view that S21043 could be used as a novel insulinotropic tool in the treatment of non-insulin-dependent diabetes mellitus, the cationic and secretory responses to the drug displaying a favourable time course for prompt and not unduly prolonged activation of islet B-cells. Copyright 1999 Academic Press.

CT Check Tags: Female

Animals

Calcium: ME, metabolism

*Calcium: PK, pharmacokinetics

Calcium Radioisotopes

Cations

*Glucose: PD, pharmacology

*Hypoglycemic Agents: PD, pharmacology

*Indoles: PD, pharmacology

*Insulin: SE, secretion

*Islets of Langerhans: DE, drug effects
 *Islets of Langerhans: ME, metabolism
 Islets of Langerhans: SE, secretion
 Perfusion
 Rats
 Rats, Wistar
 *Rubidium: PK, pharmacokinetics
 Rubidium Radioisotopes
 RN 11061-68-0 (Insulin); 50-99-7 (Glucose); 7440-17-7 (Rubidium); 7440-70-2
 (Calcium)
 CN 0 (Calcium Radioisotopes); 0 (Cations); 0 (Hypoglycemic Agents); 0
 (Indoles); 0 (Rubidium Radioisotopes); 0 (mitiglinide)

L61 ANSWER 40 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 2000280282 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 10820647
 TITLE: Recent developments and emerging therapies for type 2
 diabetes mellitus.
 AUTHOR: Evans A J; Krentz A J
 CORPORATE SOURCE: Department of Diabetes and Endocrinology, Southampton
 General Hospital, England.
 SOURCE: Drugs in R&D, (1999 Aug) Vol. 2, No. 2, pp.
 75-94. Ref: 106
 Journal code: 100883647. ISSN: 1174-5886.
 PUB. COUNTRY: New Zealand
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200008
 ENTRY DATE: Entered STN: 11 Aug 2000
 Last Updated on STN: 11 Aug 2000
 Entered Medline: 1 Aug 2000

AB Most patients with type 2 (non-insulin-dependent) diabetes mellitus require pharmacotherapy, initially as monotherapy and subsequently in combination, as adjuncts to diet and exercise. Exogenous insulin is ultimately required in a substantial proportion, reflecting the progressive natural history of the disease. Sulphonylureas and biguanides have been employed for over 4 decades as oral antidiabetic agents, but they have a limited capacity to provide long term glycaemic control and can cause serious adverse effects. Thus, more efficacious and tolerable antidiabetic agents are required. Recent years have witnessed the introduction of agents with novel modes of action, that is, the alpha-glucosidase inhibitors acarbose and miglitol (which reduce postprandial hyperglycaemia) and the first of the thiazolidinedione insulinsensitising drugs--troglitazone and rosiglitazone. Although the former has been withdrawn in some countries due to adverse effects, another 'glitazone' pioglitazone is expected to be approved in the near future. Other recently introduced drugs include glimepiride and the meglitinide insulin secretagogue, repaglinide. Attention is also focusing increasingly on combination therapy using insulin together with sulphonylureas, metformin or troglitazone. Rapid-acting insulin analogues are now being used as alternatives to conventional insulins; their role in the management of type 2 diabetes mellitus is presently uncertain but reports of a reduced frequency of hypoglycaemia are encouraging. The development of new drugs aims to counter the principal metabolic defects of the disorder; respectively, relative insulin deficiency and insulin resistance. Novel classes of rapid-acting secretagogues under evaluation include the morpholinoguanide BTS 67582 and the meglitinides mitiglinide (KAD 1229) and senaglinide (A-4166). Succinate ester derivatives represent a potential novel approach to improving beta-cell function through enhancement of insulin biosynthesis and secretion. Enhancement of nutrient-induced insulin

secretion is a mechanism with several putative targets within the beta-cell; potentiators of insulin secretion include glucagon-like peptide-1 and its analogues, phosphodiesterase inhibitors and the imidazoline derivative PMS 812 (S 21663). The amylin agonist pramlintide slows gastric emptying and suppression of glucagon secretion. Non-thiazolidinedione insulin-sensitising agents include the gamma-receptor agonist G 1262570X (GG 570) and D-chiro-inositol. Insulin analogues with prolonged action and inhaled insulin preparations are also under investigation. Insulin-mimetic agents include organic vanadium compounds. Whether newer agents will offer clinically relevant efficacy and tolerability advantages over existing therapies remains to be determined.

- CT Diabetes Mellitus, Type 2: DH, diet therapy
 *Diabetes Mellitus, Type 2: DT, drug therapy
 Humans
 Hypoglycemic Agents: AE, adverse effects
 Hypoglycemic Agents: CL, classification
 Hypoglycemic Agents: PD, pharmacology
 *Hypoglycemic Agents: TU, therapeutic use
 CN 0 (Hypoglycemic Agents)

L61 ANSWER 41 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 97041658 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 8886929
 TITLE: A rapid- and short-acting hypoglycemic agent KAD-1229 improves post-prandial hyperglycemia and diabetic complications in streptozotocin-induced non-insulin-dependent diabetes mellitus rats.
 AUTHOR: Ohnota H; Kitamura T; Kinukawa M; Hamano S; Shibata N; Miyata H; Ujije A
 CORPORATE SOURCE: Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Nagano, Japan.
 SOURCE: Japanese journal of pharmacology, (1996 Aug) Vol. 71, No. 4, pp. 315-23.
 Journal code: 2983305R. ISSN: 0021-5198.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199701
 ENTRY DATE: Entered STN: 19 Feb 1997
 Last Updated on STN: 19 Feb 1997
 Entered Medline: 30 Jan 1997

AB We investigated therapeutic effects of a rapid- and short-acting non-sulfonylurea hypoglycemic agent, calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionate dihydrate (KAD-1229), on streptozotocin (STZ)-induced non-insulin-dependent diabetes mellitus (NIDDM) rats. The effects exerted by KAD-1229 on the post-prandial plasma glucose rise in STZ-induced mild NIDDM (mNIDDM) rats were different from those of sulfonylureas. When KAD-1229 with liquid meal (10 kcal/kg) was given to the mNIDDM rats, the plasma glucose migration was similar to that of normal healthy rats. On the contrary, glibenclamide had little or no effect on the plasma glucose rise 0.5-1 hr after oral administration, and its effect was only evident 2-5 hr after dosing. Tolbutamide showed similar hypoglycemia to that induced by glibenclamide at 2-5 hr with insufficient efficacy at 0.5 hr. Gliclazide sufficiently suppressed the level of post-prandial plasma glucose. However, its complete inhibition of post-prandial plasma glucose was associated with the extra-hypoglycemia 1-5 hr after oral administration. We also tested the efficacy of KAD-1229 in more severe STZ-induced NIDDM (sNIDDM) rats to elucidate the effects of the drug on the long-term glycemic controls and

diabetic complications. When the SNIDDM rats were treated with 10 mg/kg KAD-1229 twice a day for about 17 weeks, increases in fasting plasma glucose and hemoglobin A1c were inhibited. Furthermore, treatment with KAD-1229 suppressed the development of microalbuminuria and cortical cataract. We conclude that the rapid- and short-acting insulinotropic agent KAD-1229 is able to improve the deterioration in the glycemic controls and inhibit the development of diabetic complications in STZ-induced NIDDM rats.

CT Check Tags: Male
 Albuminuria: ME, metabolism
 Analysis of Variance
 Animals
 Blood Glucose: ME, metabolism
 Diabetes Mellitus, Experimental: BL, blood
 *Diabetes Mellitus, Experimental: DT, drug therapy
 Glucagon: BL, blood
 Hyperglycemia: DT, drug therapy
 *Hypoglycemic Agents: PD, pharmacology
 *Indoles: PD, pharmacology
 Insulin: BL, blood
 Pancreas: CH, chemistry
 Pancreas: EN, enzymology
 Rats
 Rats, Sprague-Dawley
 Streptozocin
 RN 11061-68-0 (Insulin); 18883-66-4 (Streptozocin); 9007-92-5 (Glucagon)
 CN 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (mitiglinide)

L61 ANSWER 42 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 95323823 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 7600439
 TITLE: Normalization of impaired glucose tolerance by the short-acting hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionate dihydrate (KAD-1229) in non-insulin-dependent diabetes mellitus rats.
 AUTHOR: Ohnota H; Koizumi T; Kobayashi M; Momose Y; Sato F
 CORPORATE SOURCE: Creative Products Research Laboratory, Kissei Pharmaceutical Co., Ltd., Nagano-ken, Japan.
 SOURCE: Canadian journal of physiology and pharmacology, (1995 Jan) Vol. 73, No. 1, pp. 1-6.
 Journal code: 0372712. ISSN: 0008-4212.
 PUB. COUNTRY: Canada
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199508
 ENTRY DATE: Entered STN: 22 Aug 1995
 Last Updated on STN: 22 Aug 1995
 Entered Medline: 7 Aug 1995

AB We have investigated the hypoglycemic effects of the newly synthesized short-acting nonsulphonylurea hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)-propionate dihydrate (KAD-1229) in non-insulin-dependent diabetes mellitus (NIDDM) rats. NIDDM rats that were given a neonatal injection of 60 mg/kg streptozotocin showed a dose-dependent but attenuated response to oral administration of KAD-1229 and gliclazide, and their impaired glucose tolerance was improved but not normalized. We next produced, using a neonatal injection of 30 mg/kg streptozotocin, a mild type of NIDDM rat with less impaired glucose tolerance. These rats responded well to these insulinotropic hypoglycemic agents. Their impaired glucose and meal

tolerance were completely normalized by oral administration of 3 mg/kg KAD-1229. The efficacy of KAD-1229 in this NIDDM rat model 1-3 h after oral glucose administration was comparable with similar doses of gliclazide, despite its shorter hypoglycemic action (compared with gliclazide), in fasting normal rats. In meal tolerance tests (20 kcal/kg; 1 cal = 4.2 J), KAD-1229 reduced abnormally enhanced plasma glucose levels 1-3 h after administration. This effect disappeared by 5 h. In contrast, gliclazide showed sustained hypoglycemic effects until 5 h after oral administration, with a lower postprandial (0.5-1 h) effect. These data indicated that the rapid- and short-acting efficacy of KAD-1229 would be beneficial and sufficient to control postprandial plasma glucose in NIDDM rats.

CT Animals
 Animals, Newborn
*Blood Glucose: ME, metabolism
 *Diabetes Mellitus, Experimental: BL, blood
Food
Gliclazide: PD, pharmacology
Glucose Tolerance Test
*Hypoglycemic Agents: PD, pharmacology
Immunohistochemistry
*Indoles: PD, pharmacology
Pancreas: ME, metabolism
Rats
Rats, Sprague-Dawley
RN 21187-98-4 (Gliclazide)
CN 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0
 mitiglinide)

L61 ANSWER 43 OF 49 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 1

ACCESSION NUMBER: 2003324437 EMBASE Full-text
TITLE: Sulphonylurea action revisited: The post-cloning era.
AUTHOR: Gribble F.M.; Reimann F.
CORPORATE SOURCE: Dr. F.M. Gribble, Department of Clinical Biochemistry,
Addenbrooke's Hospital, Box 232, Hills Road, Cambridge, CB2
2QR, United Kingdom. fmg23@cam.ac.uk
SOURCE: Diabetologia, (1 Jul 2003) Vol. 46, No. 7, pp. 875-891. .
Refs: 163
ISSN: 0012-186X CODEN: DBTGAJ
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 2003
Last Updated on STN: 4 Sep 2003

AB Hypoglycaemic agents such as sulphonylureas and the newer group of "glinides" stimulate insulin secretion by closing ATP-sensitive potassium (K(ATP)) channels in pancreatic beta cells, but have varying cross-reactivity with related channels in extrapancreatic tissues such as heart, vascular smooth and skeletal muscle. Experiments on the structure-function relationships of recombinant K(ATP) channels and the phenotypes of mice deficient in different K(ATP) channel subunits have provided important insights into the mechanisms underlying sulphonylurea selectivity, and the potential consequences of K(ATP) channel blockade outside the pancreatic beta cell. The different pharmacological properties of K(ATP) channels from beta cells compared with

those from cardiac, smooth and skeletal muscle, are accounted for by the expression of alternative types of sulphonylurea receptor, with non-identical drug binding sites. The sulphonylureas and glinides are found to fall into two groups: one exhibiting selectivity for beta cell sulphonylurea receptors (SUR1), and the other blocking cardiovascular and skeletal muscle sulphonylurea receptors (SUR2) with potencies similar to their action on SUR1. In seeking potential side effects of K(ATP) channel inhibitors in humans, it is essential to take these drug differences into account, along with the probability (suggested by the studies on K(ATP) channel knockout mice) that the effects of extrapancreatic K(ATP) channel inhibition might be either subtle or rare. Further studies are still required before a final decision can be made on whether non-selective agents are appropriate for the therapy of Type 2 diabetes.

CT Medical Descriptors:

*non insulin dependent diabetes mellitus: DT, drug therapy

drug mechanism

drug effect

drug receptor binding

insulin release

inwardly rectifying potassium channel

pancreas islet beta cell

cross reaction

heart

vascular smooth muscle

skeletal muscle

phenotype

drug selectivity

protein expression

drug binding site

drug potency

side effect: SI, side effect

knockout mouse

medical decision making

cloning

human

nonhuman

review

priority journal

Drug Descriptors:

*sulfonylurea: AE, adverse drug reaction

*sulfonylurea: IT, drug interaction

*sulfonylurea: DT, drug therapy

*sulfonylurea: PD, pharmacology

tolbutamide: DT, drug therapy

tolbutamide: PD, pharmacology

gliclazide: DT, drug therapy

gliclazide: PD, pharmacology

 mitiglinide: DT, drug therapy

 mitiglinide: PD, pharmacology

glibenclamide: DT, drug therapy

glibenclamide: PD, pharmacology

glimepiride: DT, drug therapy

glimepiride: PD, pharmacology

repaglinide: DT, drug therapy

repaglinide: PD, pharmacology

insulin: EC, endogenous compound

adenosine triphosphate

sulfonylurea receptor: EC, endogenous compound

receptor subtype: EC, endogenous compound

chlorpropamide: DT, drug therapy

chlorpropamide: PD, pharmacology
 meglitinide: DT, drug therapy
 meglitinide: PD, pharmacology
 nateglinide: DT, drug therapy
 nateglinide: PD, pharmacology
 diazoxide: IT, drug interaction
 diazoxide: PD, pharmacology
 nicorandil: DT, drug therapy
 nicorandil: PD, pharmacology
 pinacidil
 cromakalim
RN (tolbutamide) 473-41-6, 64-77-7; (gliclazide) 21187-98-4; (mitiglinide) 145525-41-3, 207844-01-7; (glibenclamide) 10238-21-8; (glimepiride) 93479-97-1; (repaglinide) 135062-02-1; (insulin) 9004-10-8; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (chlorpropamide) 94-20-2; (meglitinide) 54870-28-9; (nateglinide) 105746-37-0, 105816-04-4, 105816-06-6; (diazoxide) 364-98-7; (nicorandil) 65141-46-0; (pinacidil) 60560-33-0; (cromakalim) 94470-67-4

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ACCESSION NUMBER: 2003422728 EMBASE Full-text

TITLE: [Current oral agents for type 2 diabetes].
TIP 2 DIYABETTE GUNCEL ORAL AJANLAR.

AUTHOR: Stoller W.A.

SOURCE: SENDROM, (2003) Vol. 15, No. 6, pp. 24-33. .
Refs: 22

ISSN: 1016-5134 CODEN: SENDEY

COUNTRY: Turkey

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: Turkish

SUMMARY LANGUAGE: English; Turkish

ENTRY DATE: Entered STN: 6 Nov 2003

Last Updated on STN: 6 Nov 2003

AB Type 2 diabetes has reached epidemic levels in the United States. Progressive evidence has emphasized the importance of glucose control in avoiding the high costs and reduced quality of life associated with the numerous complications of diabetes. Fortunately, pharmacologic options for treating type 2 diabetes have increased dramatically during the last 6 years, allowing new opportunities for successful outcomes. Such options will continue to expand. Therefore we are challenged to effectively use these agents in a logical progressive regimen while minimizing side effects.

CT Medical Descriptors:

*non insulin dependent diabetes mellitus: DT, drug therapy
*non insulin dependent diabetes mellitus: EP, epidemiology

United States

quality of life

cost of illness

pathophysiology

hypoglycemia: SI, side effect

meteorism: SI, side effect

anorexia: SI, side effect

side effect: SI, side effect

human

review

Drug Descriptors:

*oral antidiabetic agent: AE, adverse drug reaction
 *oral antidiabetic agent: DT, drug therapy
 *oral antidiabetic agent: PO, oral drug administration
 sulfonylurea: AE, adverse drug reaction
 sulfonylurea: DT, drug therapy
 sulfonylurea: PO, oral drug administration
 glibenclamide: DT, drug therapy
 glibenclamide: PO, oral drug administration
 glimepiride: DT, drug therapy
 glimepiride: PO, oral drug administration
 glipizide: DT, drug therapy
 glipizide: PO, oral drug administration
 repaglinide: AE, adverse drug reaction
 repaglinide: DT, drug therapy
 repaglinide: PO, oral drug administration
 mitiglinide: DT, drug therapy
 mitiglinide: PO, oral drug administration
 nateglinide: AE, adverse drug reaction
 nateglinide: DT, drug therapy
 nateglinide: PO, oral drug administration
 alpha glucosidase inhibitor: DT, drug therapy
 alpha glucosidase inhibitor: PO, oral drug administration
 metformin: AE, adverse drug reaction
 metformin: DT, drug therapy
 metformin: PO, oral drug administration
 insulin: DT, drug therapy
 peroxisome proliferator activated receptor agonist: AE, adverse drug reaction
 peroxisome proliferator activated receptor agonist: DT, drug therapy
 peroxisome proliferator activated receptor agonist: PO, oral drug administration
 pioglitazone: DT, drug therapy
 pioglitazone: PO, oral drug administration
 rosiglitazone: DT, drug therapy
 rosiglitazone: PO, oral drug administration
 human insulin: DT, drug therapy
 insulin glargine: DT, drug therapy
 hemoglobin A1c: EC, endogenous compound
 acarbose: AE, adverse drug reaction
 acarbose: DT, drug therapy
 acarbose: PO, oral drug administration
 miglitol: AE, adverse drug reaction
 miglitol: DT, drug therapy
 miglitol: PO, oral drug administration
 glibenclamide plus metformin
 starfix

RN (glibenclamide) 10238-21-8; (glimepiride) 93479-97-1; (glipizide) 29094-61-9; (repaglinide) 135062-02-1; (mitiglinide) 145525-41-3, 207844-01-7; (nateglinide) 105746-37-0, 105816-04-4, 105816-06-6; (metformin) 1115-70-4, 657-24-9; (insulin) 9004-10-8; (pioglitazone) 105355-27-9, 111025-46-8; (rosiglitazone) 122320-73-4, 155141-29-0; (human insulin) 11061-68-0; (insulin glargine) 160337-95-1; (hemoglobin A1c) 62572-11-6; (acarbose) 56180-94-0; (miglitol) 72432-03-2

CN Humulin; Novolin; Lantus; Glucovance; Prandin; Starfix; Precose; Glyset

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ACCESSION NUMBER: 2004050138 EMBASE Full-text
 TITLE: World Congress of Pharmacology - XIVth Annual Meeting: New

AUTHOR: drugs I: 7-12 July 2002, San Francisco, CA, USA.
 Waterworth C.; Durrance A.
 CORPORATE SOURCE: C. Waterworth, Current Drugs Ltd., Middlesex House, 34-42
 Cleveland Street, London W1T 4LB, United Kingdom.
 charlotte.waterworth@current.drugs.com
 SOURCE: IDRugs, (2002) Vol. 5, No. 8, pp. 745-748. .
 ISSN: 1369-7056 CODEN: IDRUFN
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Conference Article
 FILE SEGMENT: 037 Drug Literature Index
 029 Clinical Biochemistry
 025 Hematology
 030 Pharmacology
 018 Cardiovascular Diseases and Cardiovascular Surgery
 LANGUAGE: English
 ENTRY DATE: Entered STN: 12 Feb 2004
 Last Updated on STN: 12 Feb 2004

CT Medical Descriptors:

- human
- clinical trial
- nonhuman
- protein targeting
- thrombocyte aggregation
- kidney function
- diabetes mellitus
- Alzheimer disease
- drug potency
- drug activity
- drug structure
- drug dose regimen
- thrombosis: DT, drug therapy
- atherosclerosis: DT, drug therapy
- drug effect
- obesity: DT, drug therapy
- dose response
- area under the curve
- cognitive defect: DT, drug therapy
- drug metabolism
- drug half life
- drug bioavailability
- drug blood level
- glaucoma: DT, drug therapy
- tumor: DT, drug therapy
- conference paper

CT Drug Descriptors:

- *new drug: PD, pharmacology
- *new drug: AN, drug analysis
- *new drug: DO, drug dose
- *new drug: CM, drug comparison
- *new drug: DT, drug therapy
- *new drug: PO, oral drug administration
- *new drug: CT, clinical trial
- *new drug: PK, pharmacokinetics
- *new drug: CR, drug concentration
- purine P2Y receptor: EC, endogenous compound
- antithrombocytic agent: PD, pharmacology
- antithrombocytic agent: AN, drug analysis
- antithrombocytic agent: DO, drug dose
- antithrombocytic agent: CM, drug comparison
- antithrombocytic agent: DT, drug therapy

dinucleoside polyphosphate inhibitor: PD, pharmacology
 dinucleoside polyphosphate inhibitor: AN, drug analysis
 dinucleoside polyphosphate inhibitor: DO, drug dose
 dinucleoside polyphosphate inhibitor: CM, drug comparison
 dinucleoside polyphosphate inhibitor: DT, drug therapy
 peroxisome proliferator activated receptor agonist: DT, drug therapy
 peroxisome proliferator activated receptor agonist: PD, pharmacology
 peroxisome proliferator activated receptor agonist: CM, drug comparison
 peroxisome proliferator activated receptor agonist: AN, drug analysis
 acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: DT, drug therapy
 acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: CM, drug comparison
 acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: PD, pharmacology
 mitiglinide: DT, drug therapy
 mitiglinide: PD, pharmacology
 mitiglinide: PK, pharmacokinetics
 mitiglinide: DO, drug dose
 mitiglinide: AN, drug analysis
 peptide derivative: DT, drug therapy
 peptide derivative: CT, clinical trial
 peptide derivative: PD, pharmacology
 peptide derivative: AN, drug analysis
 noopept: DT, drug therapy
 noopept: CT, clinical trial
 noopept: PD, pharmacology
 noopept: AN, drug analysis
 pirfenidone: DT, drug therapy
 pirfenidone: CT, clinical trial
 pirfenidone: PK, pharmacokinetics
 pirfenidone: IV, intravenous drug administration
 pirfenidone: DO, drug dose
 pirfenidone: AN, drug analysis
 nitronaproxen: DT, drug therapy
 nitronaproxen: PK, pharmacokinetics
 nitronaproxen: PO, oral drug administration
 nitronaproxen: CR, drug concentration
 nitronaproxen: PD, pharmacology
 nitronaproxen: AN, drug analysis
 6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: DT,
 drug therapy
 6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: CT,
 clinical trial
 6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: AN,
 drug analysis
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT,
 drug therapy
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD,
 pharmacology
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT,
 clinical trial
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DO,
 drug dose
 2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PK,
 pharmacokinetics
 antiglaucoma agent: DT, drug therapy
 antiglaucoma agent: CT, clinical trial
 antiglaucoma agent: PD, pharmacology
 antineoplastic agent: DT, drug therapy
 antineoplastic agent: PD, pharmacology
 nitrostyrene derivative: DT, drug therapy
 nitrostyrene derivative: PD, pharmacology

endothelin converting enzyme inhibitor: DT, drug therapy
endothelin converting enzyme inhibitor: PD, pharmacology
cgs 35066: DT, drug therapy
cgs 35066: PD, pharmacology
bis (7 tacrine): DT, drug therapy
bis (7 tacrine): PD, pharmacology
bis (7 tacrine): AN, drug analysis
bis (7 tacrine): DO, drug dose
conivaptan: DT, drug therapy
conivaptan: PD, pharmacology
conivaptan: CB, drug combination
conivaptan: AN, drug analysis
conivaptan: CM, drug comparison
conivaptan: DO, drug dose
carbamic acid derivative: PD, pharmacology
carbamic acid derivative: AN, drug analysis
carbamic acid derivative: DO, drug dose
carbamic acid derivative: CM, drug comparison
carbamic acid derivative: DT, drug therapy
diquafosol: PD, pharmacology
diquafosol: CM, drug comparison
diquafosol: DT, drug therapy
ns 220: DT, drug therapy
ns 220: PD, pharmacology
ns 220: CM, drug comparison
ns 220: AN, drug analysis
fenofibrate: DT, drug therapy
fenofibrate: PD, pharmacology
fenofibrate: CM, drug comparison
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: PD, pharmacology
a 331440: DT, drug therapy
a 331440: PO, oral drug administration
a 331440: DO, drug dose
a 331440: CM, drug comparison
a 331440: PD, pharmacology
dexfenfluramine: DT, drug therapy
dexfenfluramine: CM, drug comparison
dexfenfluramine: PD, pharmacology
thioperamide: DT, drug therapy
thioperamide: CM, drug comparison
thioperamide: PD, pharmacology
ciprofloxacin: DT, drug therapy
ciprofloxacin: CM, drug comparison
ciprofloxacin: PD, pharmacology
unindexed drug
unclassified drug
ins 48372
ins 46116
ins 46117
ins 46061
ins 46058
ins 48795
ins 40150
ins 40270
ins 46060
ins 49162
ins 46059
s 35836 1

s 35678 1
 gvs 111
 ot 7999
 RN (acetylsalicylic acid 3 (nitroxymethyl)phenyl ester) 190442-10-5; (mitiglinide) 145525-41-3, 207844-01-7; (pirfenidone) 53179-13-8; (nitronaproxen) 163133-43-5; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (conivaptan) 168626-94-6, 210101-16-9; (diquafosol) 211427-08-6; (fenofibrate) 49562-28-9; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (dexfenfluramine) 3239-44-9, 3239-45-0; (thioperamide) 106243-16-7; (ciprofloxacin) 85721-33-1
 CN (1) Ins 48372; (2) Ins 46116; (3) Ins 46117; (4) Ins 46061; (5) Ins 46058; (6) Ins 48795; (7) Ins 40150; (8) Ins 40270; (9) Ins 46060; (10) Ins 49162; (11) Ins 46059; (12) Ins 365; (13) Ns 220; (14) A 331440; (15) Kad 1229; (16) Kad 1229; (17) S 35836 1; (18) S 35678 1; (19) Kad 1229; (20) Gvs 111; (21) Azd 3582; (22) Azd 3582; (23) Ncx 4016; (24) Pnu 142721; (25) Su 6668; (26) Ot 7999; (27) Cgs 35066; (28) Ym 087; (29) Ym 087; (30) Amr 69; (31) Amr 69; (32) Amr 69; (33) Amr 69
 CO (12) Inspire; (13) Nippon Shinyaku; (14) Abbott; (15) Kissei; (18) Servier; (19) Takeda; (20) Russian Academy of Sciences; (21) Astra Zeneca; (23) Nicox; (24) Pharmacia (United States); (25) Sugen; (26) Otsuka; (27) Novartis; (28) Yamanouchi; (29) Pfizer; (30) Marnac; (31) Intermune; (32) Schering AG; (33) Shionogi; UCB

L61 ANSWER 46 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2003-08972 DRUGU T S E Full-text

TITLE: Diabetes and insulin resistance associated disorders: disease and the therapy.
 AUTHOR: Chakrabarti R; Rajagopalan R
 CORPORATE SOURCE: Dr.Reddy's-Lab.
 LOCATION: Hyderabad, India
 SOURCE: Curr.Sci. (83, No. 12, 1533-38, 2002) 2 Fig. 2 Tab. 18 Ref.
 CODEN: CUSCAM ISSN: 0011-3891
 AVAIL. OF DOC.: Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India. (R.R.). (e-mail: rajagopalanr@drreddys.com).
 LANGUAGE: English
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature
 AB The therapy of diabetes and insulin resistance associated disorders are reviewed. Topics covered are classes of currently available drugs and future targets. Established drugs and those in trials discussed are acetohehexamide, chlorpropamide, tolbutamide, tolazamide, glyburide, glipizide, glimiperide, repaglinide, nateglinide, glibenclamide, mitiglinide, metformin, phenformin, cigitazone, troglitazone, rosiglitazone, pioglitazone, acarbose, miglitol (side-effects of these drugs were also mentioned), balaglitazone, natoglitazone, ragaglitazar, tesagliptazar, KRP-297, BMS-298585, regagliptazar, SR-58611, TAK-677, GP-3034, LAF-237, P-32-98, DPP-728 and NN-2211. Current research efforts are focussed on insulin sensitizers, PPAR agonists, protein tyrosine phosphatase inhibitors, beta-3 adrenoceptor agonists, inhibitors of hepatic glucose output and insulin secretagogues. (No EX).

AN 2003-08972 DRUGU T S E Full-text
 T Therapeutics
 S Adverse Effects
 E Endocrinology
 12 Antidiabetics
 35 Adverse Reactions
 64 Clinical Trials
 69 Reviews

73 Trial Preparations
 CT DIABETES *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY
 *TR; CASES *FT; IN-VIVO *FT; ANTIDIABETIC *FT; CLIN.TRIAL *FT; REVIEW
 *FT
 [01] MAIN-TOPIC *FT; ANTIDIABETICS *FT; TR *FT; AE *FT
 [02] ACETOHEXAMIDE *TR; CHLORPROPAMIDE *TR; TOLBUTAMIDE *TR; TOLAZAMIDE
 *TR; GLIBENCLAMIDE *TR; GLIPIZIDE *TR; GLIMIPERIDE *TR; REPAGLINIDE
 *TR; NATEGLINIDE *TR; GLIBENCLAMIDE *TR; MITIGLINIDE *TR;
 METFORMIN *TR; PHENFORMIN *TR; CIGLITAZONE *TR; TROGLITAZONE *TR;
 ROSIGLITAZONE *TR; PIOGLITAZONE *TR; ACARBOSE *TR; MIGLITOL *TR;
 BALAGLITAZONE *TR; NATOGLITAZONE *TR; RAGAGLITAZAR *TR; TESAGLITAZAR
 *TR; KRP-297 *TR; BMS-298585 *TR; REGAGLITAZAR *TR; SR-58611 *TR;
 TAK-677 *TR; GP-3034 *TR; LAF-237 *TR; P-32-98 *TR; DPP-728 *TR;
 NN-2211 *TR; TR *FT
 [03] ACETOHEXAMIDE *AE; CHLORPROPAMIDE *AE; TOLBUTAMIDE *AE; TOLAZAMIDE
 *AE; GLIBENCLAMIDE *AE; GLIPIZIDE *AE; GLIMIPERIDE *AE; REPAGLINIDE
 *AE; NATEGLINIDE *AE; GLIBENCLAMIDE *AE; MITIGLINIDE *AE;
 METFORMIN *AE; PHENFORMIN *AE; CIGLITAZONE *AE; TROGLITAZONE *AE;
 ROSIGLITAZONE *AE; PIOGLITAZONE *AE; ACARBOSE *AE; MIGLITOL *AE;
 BALAGLITAZONE *AE; NATOGLITAZONE *AE; RAGAGLITAZAR *AE; TESAGLITAZAR
 *AE; KRP-297 *AE; BMS-298585 *AE; REGAGLITAZAR *AE; SR-58611 *AE;
 TAK-677 *AE; GP-3034 *AE; LAF-237 *AE; P-32-98 *AE; DPP-728 *AE;
 NN-2211 *AE; AE *FT

L61 ANSWER 47 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2002-33933 DRUGU P E Full-text
 TITLE: Clinical pharmacokinetics and pharmacodynamics of
 repaglinide.
 AUTHOR: Hatorp V
 LOCATION: Hoersholm, Den.
 SOURCE: Clin.Pharmacokinet. (41, No. 7, 471-83, 2002) 5 Fig. 4 Tab.

48 Ref.

AVAIL. OF DOC.: CODEN: CPKNDH ISSN: 0312-5963
 Danish Toxicology Center, Kogle Alle 2, DK-2970 Hoersholm,
 Denmark. (e-mail: vh@dtc.dk).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Clinical pharmacokinetics and pharmacodynamics of repaglinide (RP) are reviewed. The pharmacokinetics of RP in healthy volunteers, patients with type 2 diabetes, and in special populations (hepatic and renal insufficiency) are analyzed. Drug-drug interactions are presented with reference to protein binding interactions and in-vivo interactions with cimetidine, digoxin, theophylline, warfarin, and rifampicin. Finally, the pharmacodynamics of RP are discussed in relation to dose tolerance, dose response and dosage regimen.

AN 2002-33933 DRUGU P E Full-text

P Pharmacology

E Endocrinology

8 Pharmacokinetics

12 Antidiabetics

66 Drug Interactions

69 Reviews

CT CASES *FT; HUMAN *FT; IN-VIVO *FT; REVIEW *FT; PHARMACOKINETICS *FT;
 PHARMACODYNAMICS *FT; ANTIDIABETIC *FT

[01] REPAGLINIDE *PH; REPAGLINIDE *DM; AGEE623ZW *RN; MAIN-TOPIC *FT;
 ANTIDIABETICS *FT; PH *FT; DM *FT

RN: 135062-02-1

[02] NATEGLINIDE *PH; MITIGLINIDE *PH; KETOCONAZOLE *DI;

RIFAMPICIN *DI; CIMETIDINE *DI; DIGOXIN *DI; THEOPHYLLINE *DI;
WARFARIN *DI; PH *FT; DI *FT

L61 ANSWER 48 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2003-11212 DRUGU P E Full-text
 TITLE: Sulfonylurea stimulation of insulin secretion.
 AUTHOR: Proks P; Reimann F; Green N; Gribble F; Ashcroft F
 CORPORATE SOURCE: Univ.Oxford; Univ.Cambridge
 LOCATION: Oxford; Cambridge, U.K.
 SOURCE: Diabetes (51, Suppl. 3, S368-S376, 2002) 4 Fig. 1 Tab. 55
 Ref.
 CODEN: DIAEAZ ISSN: 0012-1797
 AVAIL. OF DOC.: University Laboratory of Physiology, Parks Road, Oxford OX1
 3PT, England. (F.A.). (e-mail: frances.ashcroft@physiol.ox.ac.uk).
 LANGUAGE: English
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature
 AB Sulfonylurea stimulation of insulin secretion is reviewed. The inhibition of KATP channels by imidazolines (phentolamine, cibenzoline), antimalarials (quinine, mefloquine), sulfonylureas (tolbutamide, gliclazide, glimepiride), and benzamido derivatives and the specificity of high-affinity sulfonylurea block are discussed. The location of the sulfonylurea binding site on SUR and interactions between Kir6.1 and SUR are explained. Modulation of sulfonylurea block by PIP2 and modulation of sulfonylurea block by MG nucleotides are considered. Findings indicate that the classification of sulfonylureas, meglitinide derivatives etc can be changed to reflect the functional differences among these drugs, and that they be referred to instead as SUR1-specific and non-SUR1-specific. (conference paper: 3rd Servier - IGIS Symposium, St. Jean Cap Ferrat, France, 2002).
 AN 2003-11212 DRUGU P E Full-text
 P Pharmacology
 E Endocrinology
 12 Antidiabetics
 69 Reviews
 CT REVIEW *FT; INSULIN *FT; PANCREAS-HORMONE-METAB. *FT; ANTIDIABETIC *FT; MODE-OF-ACT. *FT; IN-VIVO *FT; LAB.ANIMAL *FT
 [01] MAIN-TOPIC *FT; ANTIDIABETICS *FT; PH *FT
 [02] PHENTOLAMINE *PH; CIBENZOLINE *PH; QUININE *PH; MEFLOQUINE *PH; TOLBUTAMIDE *PH; GLICLAZIDE *PH; GLIMEPIRIDE *PH; MEGLITINIDE *PH; MITIGLINIDE *PH; NATEGLINIDE *PH; GLIBENCLAMIDE *PH; GLIPIZIDE *PH; REPAGLINIDE *PH; PH *FT
 L61 ANSWER 49 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2001-42236 DRUGU P T E Full-text
 TITLE: Insulinotropic maglitinide analogues.
 AUTHOR: Dornhorst A
 CORPORATE SOURCE: Univ.London
 LOCATION: London, U.K.
 SOURCE: Lancet (358, No. 9294, 1709-16, 2001) 3 Fig. 78 Ref.
 CODEN: LANCAO ISSN: 0140-6736
 AVAIL. OF DOC.: Department of Metabolic Medicine, Faculty of Medicine, Imperial College, Hammersmith Hospital Campus, Du Cane Road, London W12 0NN, England. (e-mail: a.dornhorst@ic.ac.uk).
 LANGUAGE: English
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature

- AB Insulinotropic meglitinide analogs are reviewed in terms of the pathophysiology of type 2 diabetes and the importance of beta cell function, defects in insulin pulsatility and early-phase insulin secretion in those at risk of type 2 diabetes. Pharmacological approaches to type 2 diabetes are discussed and the mechanism of action, efficacy in clinical trials, combination therapy and pharmacokinetics, safety and tolerability of repaglinide and nateglinide are explored in detail. The ability to preserve beta cell function is compared in nateglinide and glibenclamide. Mitiglinide is also briefly considered along with an evaluation of recent mixed molecules such as BTS-67582. Understanding of the pathophysiology of type 2 diabetes is now clearer and this knowledge is beginning to yield new agents of therapeutic promise such as repaglinide and nateglinide.
- AN 2001-42236 DRUGU P T E Full-text
 P Pharmacology
 T Therapeutics
 E Endocrinology
 12 Antidiabetics
 64 Clinical Trials
 69 Reviews
- CT DIABETES *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY *TR; REVIEW *FT; IN-VITRO *FT; IN-VIVO *FT; CASES *FT; LAB.ANIMAL *FT; BETA-CELL *FT; PHARMACOKINETICS *FT; MODE-OF-ACT. *FT; INSULIN *FT; CARBOHYDRATE-METAB. *FT; CLIN.TRIAL *FT; COMB. *FT; ANTIDIABETIC *FT; PANCREAS *FT
- [01] MAIN-TOPIC *FT; ANTIDIABETICS *FT; TR *FT; PH *FT
- [02] MEGLITINIDE *TR; REPAGLINIDE *TR; METFORMIN *TR; TROGLITAZONE *TR; NATEGLINIDE *TR; MITIGLINIDE *TR; BTS-67582 *TR; S-21663 *PH; S-2166 *PH; JTT-608 *PH; MEGLITINIDE *PH; REPAGLINIDE *PH; METFORMIN *PH; TROGLITAZONE *PH; NATEGLINIDE *PH; MITIGLINIDE *PH; BTS-67582 *PH; GLIBENCLAMIDE *PH; TR *FT; PH *FT

10/519155

***** INVENTOR RESULTS *****

=> d his 142

(FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007)

L42 6 S L41 NOT L33

=> d que 142

| | | | |
|-----|---------------------------------|--|---|
| L4 | 1 SEA FILE=REGISTRY ABB=ON | PLU=ON | 145375-43-5/RN |
| L5 | 1 SEA FILE=REGISTRY ABB=ON | PLU=ON | 207844-01-7/RN |
| L6 | 1 SEA FILE=REGISTRY ABB=ON | PLU=ON | MITIGLINIDE/CN |
| L8 | 2 SEA FILE=REGISTRY ABB=ON | PLU=ON | (L4 OR L5 OR L6) |
| L9 | 97 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L8 OR MITIGLINIDE CALCIUM
HYDRATE/OBI |
| L10 | 87 SEA FILE=HCAPLUS ABB=ON | PLU=ON | MITIGLINIDE/OBI OR MITI/OBI(W)
GLINIDE/OBI |
| L11 | 108 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L9 OR L10 |
| L13 | 2160940 SEA FILE=HCAPLUS ABB=ON | PLU=ON | (INHIBIT?/OBI OR HINDER?/OBI
OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI) |
| L19 | 110617 SEA FILE=HCAPLUS ABB=ON | PLU=ON | DIABET?/OBI |
| L20 | 54 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L11 AND L19 |
| L22 | 28 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L13 (5A) L20 |
| L23 | QUE ABB=ON PLU=ON | AY<2004 OR PRY<2004 OR PY<2004 OR MY
<2004 OR REVIEW/DT | |
| L24 | 17 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L22 AND L23 |
| L27 | 271 SEA FILE=HCAPLUS ABB=ON | PLU=ON | HYPERGLYCEM?/OBI (3A)
(POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI) |
| L28 | 3 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L11 AND L27 |
| L29 | 13237 SEA FILE=HCAPLUS ABB=ON | PLU=ON | HYPERGLYCEM?/OBI |
| L30 | 13237 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L27 OR L29 |
| L31 | 7 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L11 AND L30 |
| L32 | 7 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L28 OR L31 |
| L33 | 24 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L32 OR L24 |
| L34 | 15 SEA FILE=HCAPLUS ABB=ON | PLU=ON | "MIKOSHIBA IMAO"/AU |
| L35 | 328 SEA FILE=HCAPLUS ABB=ON | PLU=ON | SUZUKI HISAO/AU |
| L36 | 9 SEA FILE=HCAPLUS ABB=ON | PLU=ON | KIYONO YUJI/AU |
| L37 | 346 SEA FILE=HCAPLUS ABB=ON | PLU=ON | (L34 OR L35 OR L36) |
| L38 | 673 SEA FILE=HCAPLUS ABB=ON | PLU=ON | ("KISSEI PHARMACEUTICAL"/CO
OR "KISSEI PHARMACEUTICAL"/PA OR "KISSEI PHARMACEUTICAL"/CS OR
"KISSEI PHARMACEUTICAL CO"/CO OR "KISSEI PHARMACEUTICAL CO
LTD"/CO OR "KISSEI PHARMACEUTICAL CO LTD"/PA OR "KISSEI
PHARMACEUTICAL CO LTD"/CS OR "KISSEI PHARMACEUTICAL CO LTD
CENTRAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO
LTD CENTRAL RESEARCH LABORATORIES HOTAKA 399 83 JAPAN"/CS OR
"KISSEI PHARMACEUTICAL CO LTD JAPAN"/PA OR "KISSEI PHARMACEUTIC
AL CO LTD JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD NAGANO
399 8304 JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD PHARMACEUTI
CAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO LTD
PHARMACEUTICAL RESEARCH LABORATORIES NAGANO 399 8304 JAPAN"/CS
OR "KISSEI PHARMACEUTICAL CO LTD SHINSHU UNIVERSITY"/CO OR
"KISSEI PHARMACEUTICAL COMPANY"/CO OR "KISSEI PHARMACEUTICAL
COMPANY LIMITED"/CO OR "KISSEI PHARMACEUTICAL COMPANY LTD"/CO
OR "KISSEI PHARMACEUTICAL INDUSTRY CO LTD"/CO OR "KISSEI
PHARMACEUTICAL JAPAN"/PA OR "KISSEI PHARMACEUTICAL JAPAN"/CS) |
| L39 | 722 SEA FILE=HCAPLUS ABB=ON | PLU=ON | KISSEI PHARMA?/PA,CS,CO |
| L40 | 722 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L38 OR L39 |
| L41 | 8 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L37 AND L40 |
| L42 | 6 SEA FILE=HCAPLUS ABB=ON | PLU=ON | L41 NOT L33 |

10/519155

=> d his 160

(FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007)
L60 6 S L59 NOT L49

=> d que 160

L4 1 SEA FILE=REGISTRY ABB=ON PLU=ON 145375-43-5/RN
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON 207844-01-7/RN
L6 1 SEA FILE=REGISTRY ABB=ON PLU=ON MITIGLINIDE/CN
L8 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L4 OR L5 OR L6)
L10 87 SEA FILE=HCAPLUS ABB=ON PLU=ON MITIGLINIDE/OBI OR MITI/OBI(W)
GLINIDE/OBI
L13 2160940 SEA FILE=HCAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR HINDER?/OBI
OR IMPEDE?/OBI OR REDUCE?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
PREVENT?/OBI OR BLOCK?/OBI OR ELIMINATE?/OBI)
L19 110617 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABET?/OBI
L23 QUE ABB=ON PLU=ON AY<2004 OR PRY<2004 OR PY<2004 OR MY
<2004 OR REVIEW/DT
L27 271 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI (3A)
(POST/OBI(W) PRANDIAL/OBI OR POSTPRANDIAL/OBI)
L29 13237 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPERGLYCEM?/OBI
L43 84 SEA L8
L44 172 SEA L10
L45 10 SEA MITIGLINIDE CALCIUM HYDRATE
L46 173 SEA (L43 OR L44 OR L45)
L47 110 SEA L46 AND (L19 OR L27 OR L29)
L48 46 SEA L47 AND L23
L49 33 SEA L48 (P) L13
L50 27 SEA MIKOSHIBA I?/AU
L52 34 SEA SUZUKI HISAO/AU
L53 2 SEA KIYONO YUJI/AU
L54 63 SEA L50 OR L52 OR L53
L55 2 SEA L50 AND L52 OR L53
L56 2 SEA L54 AND L46
L57 2 SEA L55 OR L56
L58 6 SEA L54 AND (L19 OR L27 OR L29)
L59 6 SEA L57 OR L58
L60 6 SEA L59 NOT L49

=> dup rem 142 160

PROCESSING COMPLETED FOR L42

PROCESSING COMPLETED FOR L60

L62 10 DUP REM L42 L60 (2 DUPLICATES REMOVED)
ANSWERS '1-6' FROM FILE HCAPLUS
ANSWER '7' FROM FILE MEDLINE
ANSWER '8' FROM FILE BIOSIS
ANSWER '9' FROM FILE EMBASE
ANSWER '10' FROM FILE DRUGU

=> d 162 1-6 ibib abs

L62 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:836630 HCAPLUS Full-text
DOCUMENT NUMBER: 142:384723
TITLE: Pharmacological and clinical profile of mitiglinide
calcium hydrate (Glufast), a new insulinotropic agent
with rapid onset
AUTHOR(S): Ojima, Kazuma; Kiyono, Yuji; Kojima, Masami

CORPORATE SOURCE: Pharmacol. Res. Lab. R & D, Kissei Pharm. Co., Ltd., Nagano, 399-8304, Japan
 SOURCE: Nippon Yakurigaku Zasshi (2004), 124(4), 245-255
 CODEN: NYKZAU; ISSN: 0015-5691
 PUBLISHER: Nippon Yakuri Gakkai
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Japanese

AB A review. Mitiglinide calcium hydrate (mitiglinide, Glufast) is a new insulinotropic agent of the glinide class with rapid onset. Mitiglinide is thought to stimulate insulin secretion by closing the ATP-sensitive K⁺ (KATP) channels in pancreatic β-cells, and its early insulin release and short duration of action would be effective in improving postprandial hyperglycemia. In studies of various cloned KATP channels, mitiglinide shows a higher selectivity for the β-cell type of SUR1/Kir6.2 than the cardiac and smooth muscle types of KATP channels in comparison with glibenclamide and glimepiride. In vitro and in vivo studies demonstrated the insulinotropic effect of mitiglinide is more potent than that of nateglinide, and mitiglinide surpassed in controlling postprandial hyperglycemia in normal and diabetic animals. In clin. trials, treatment with mitiglinide provided lasting improvement of postprandial hyperglycemia in Type 2 diabetic patients and decreased the fasting plasma glucose levels and HbA1C values. The incidence of adverse events related to mitiglinide were nearly equivalent to placebo; in particular there was no difference with the frequency of hypoglycemia. The results from these studies indicated that mitiglinide could be expected to possess good therapeutic features of being effective in reducing postprandial glucose excursions in the early stage of Type 2 diabetes and less incidence of events suggestive of hypoglycemia.

L62 ANSWER 2 OF 10 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2007:404898 HCPLUS Full-text
 DOCUMENT NUMBER: 146:372816
 TITLE: Mitglinide and α-glucosidase inhibitor combination for type 2 diabetes therapy
 INVENTOR(S): Kiyono, Yuji; Okubo, Yoshio; Mototani, Katsumi; Mikoshiba, Imao
 PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 11pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| JP 2007091641 | A | 20070412 | JP 2005-283608 | 20050929 |
| PRIORITY APPLN. INFO.: | | | JP 2005-283608 | 20050929 |

AB Disclosed are a pharmaceutical preparation for controlling the condition of type 2 diabetes comprising the combination of mitiglinide or a pharmacol. acceptable salt or hydrate thereof and an α-glycosidase inhibitor, e.g., voglibose. The pharmaceutical preparation shows a potent effect of decreasing the morning fasting blood glucose level, the postprandial blood glucose level and HbA1c in a patient with type 2 diabetes and can ameliorate insulin resistance.

L62 ANSWER 3 OF 10 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2006:1157536 HCPLUS Full-text

DOCUMENT NUMBER: 145:477898
 TITLE: Combined pharmaceutical preparation for treatment of type 2 diabetes
 INVENTOR(S): Kiyono, Yuji; Okubo, Yoshio; Hontani, Katsumi; Mikoshiba, Imao; Ojima, Kazuma
 PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 29pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|------------|
| WO 2006115115 | A1 | 20061102 | WO 2006-JP308110 | 20060418 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |
| PRIORITY APPLN. INFO.: | | | JP 2005-121862 | A 20050420 |
| | | | JP 2005-166314 | A 20050607 |

AB Disclosed are a pharmaceutical preparation for controlling the condition of type 2 diabetes, the pharmaceutical preparation comprising the combination of metiglinide or a pharmacol. acceptable salt or hydrate thereof and an α -glycosidase inhibitor (e.g., voglibose, acarbose); and a therapeutic method using the pharmaceutical preparation. The pharmaceutical preparation shows an extremely potent effect of decreasing the morning fasting blood glucose level, the postprandial blood glucose level and HbA1c in a patient with type 2 diabetes and can ameliorate glucose spike, insulin resistance and lipid metabolism.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

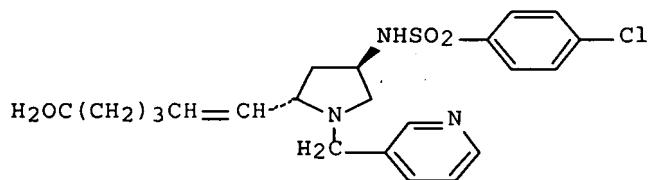
L62 ANSWER 4 OF 10 HCPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1996:83073 HCPLUS Full-text
 DOCUMENT NUMBER: 124:165270
 TITLE: Therapeutics for peripheral circulation disorders containing (pyridylmethyl)pyrrolidine derivative
 INVENTOR(S): Mikoshiba, Imao; Myata, Hiroshi; Komatsu, Hidetada; Hoyano, Takeshi; Kiguchi, Sumyoshi
 PATENT ASSIGNEE(S): Kissei Pharmaceutical, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 07304671 | A | 19951121 | JP 1994-130781 | 19940509 |

PRIORITY APPLN. INFO.:
GI

JP 1994-130781

19940509



AB Therapeutics for symptoms caused by peripheral circulation disorders contain the title derivative (I) or its pharmacol. acceptable salts. The therapeutics are useful for treatment of rhigosis (cool sensation), numbness, and pain. I.HCl (preparation given) significantly improved neurotransmission rate in rats with streptozotocin-induced peripheral circulation disorder.

L62 ANSWER 5 OF 10 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:115295 HCPLUS Full-text
 DOCUMENT NUMBER: 88:115295
 TITLE: Effect of a combined preparation of aluminum dihydroxyallantoinate and meta-magnesium aluminosilicate (Alanta) on acute gastritis in beagles
 AUTHOR(S): Azuma, Hiroshi; Shibata, Nobuo; Mikoshiba, Imao; Minamide, Seiki; Naito, Jun; Matsuda, Kuniaki; Kumazawa, Nariyuki
 CORPORATE SOURCE: Div. Pharmacol., Kissei Pharm. Co., Ltd., Matsumoto City, Japan
 SOURCE: Oyo Yakuri (1977), 13(3), 389-98
 CODEN: OYYAA2; ISSN: 0369-8033
 DOCUMENT TYPE: Journal
 LANGUAGE: Japanese
AB The inhibitory effect of Alanta [65775-48-6] on gastritis was demonstrated by histol. examination and also by determination of fibrinolysis.

L62 ANSWER 6 OF 10 HCPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:99164 HCPLUS Full-text
 DOCUMENT NUMBER: 88:99164
 TITLE: Pharmacological analysis of the combined effect of aluminum dihydroxyallantoinate and meta-magnesium aluminosilicate
 AUTHOR(S): Azuma, Hiroshi; Naito, Jun; Tamaoki, Hiroshi; Amaki, Masaharu; Mikoshiba, Imao; Akahane, Masuo
 CORPORATE SOURCE: Div. Pharmacol., Kissei Pharm. Co. Ltd., Matsumoto City, Japan
 SOURCE: Oyo Yakuri (1977), 13(3), 383-7
 CODEN: OYYAA2; ISSN: 0369-8033
 DOCUMENT TYPE: Journal
 LANGUAGE: Japanese
AB Aldioxa [5579-81-7] (Al dihydroxyallantoinate) dose-dependently inhibited stress-induced ulcer in rats. The ED50 of the drug was 523 mg/kg. A slight

inhibition of the stress-induced ulcer was elicited by treatment with metamagnesium aluminosilicate (MAS) [1327-43-1]. The ED50 of MAS was 25,500 mg/kg. When aldioxa and MAS were administered in combination in the ratio of 1/9, 1/19 and 1/29, the ED50 values were 1194, 1819 and 5725 mg/kg, resp. The inhibitory effect on the water immersion stress-induced ulcer was also potentiated by combined treatment with aldioxa and MAS. Aldioxa and MAS inhibited pylorus-ligation-induced ulcer in a dose-dependent manner. The ED50 values were 446 and 406 mg/kg, resp. When aldioxa and MAS were administered in the ratio of 1/9, 1/1 and 2/1, the ED50 values were 369, 395, and 405 mg/kg, resp. The inhibitory effect on pylorus-ligation ulcer induction was enhanced in an additive manner by the combined treatment.

=> d 162 7-10 ibib ab

L62 ANSWER 7 OF 10 MEDLINE on STN

ACCESSION NUMBER: 2003177108 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12694990

TITLE: Rationale and evidence for the use of oxcarbazepine in neuropathic pain.

AUTHOR: Carrazana Enrique; Mikoshiba Imao

CORPORATE SOURCE: Neuroscience, Clinical Development and Medical Affairs, Novartis Pharmaceuticals, East Hanover, NJ 07936-1080, USA.

SOURCE: Journal of pain and symptom management, (2003 May) Vol. 25, No. 5 Suppl, pp. S31-5. Ref: 25

Journal code: 8605836. ISSN: 0885-3924.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200307

ENTRY DATE: Entered STN: 17 Apr 2003

Last Updated on STN: 3 Jul 2003

Entered Medline: 2 Jul 2003

AB Oxcarbazepine is a second-generation antiepileptic drug (AED) with proven efficacy in managing partial epileptic seizures, with or without secondary generalization, in adults and children. The overlap between the underlying pathophysiologic mechanisms of some epilepsy models and neuropathic pain models supports the rationale for using certain AEDs in the treatment of neuropathic pain. Several AEDs have reportedly produced analgesia in a range of neuropathic pains, including painful diabetic neuropathy (PDN) and post-herpetic neuralgia. Increasing evidence suggests that oxcarbazepine can provide significant analgesia in several neuropathic pain conditions, including trigeminal neuralgia and PDN, and is also may be effective in treating neuropathic pain refractory to other AEDs, such as carbamazepine and gabapentin. The analgesic effects of oxcarbazepine, and its generally improved safety and tolerability profile compared with other standard AEDs, suggests that oxcarbazepine will be an important addition to the neuropathic pain armamentarium. The rationale and evidence to support the efficacy of oxcarbazepine are presented here.

L62 ANSWER 8 OF 10 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:442810 BIOSIS Full-text

DOCUMENT NUMBER: PREV200000442810

TITLE: Re-evaluation of exercise prescription for Japanese type 2 diabetic patients by ventilatory threshold.

AUTHOR(S): Kunitomi, Mie [Reprint author]; Takahashi, Kayo; Wada, Jun; Suzuki, Hisao; Miyatake, Nobuyuki; Ogawa, Saeko; Ohta, Sachiko; Sugimoto, Hikaru; Shikata, Kenichi; Makino, Hirofumi

CORPORATE SOURCE: Department of Medicine III, Okayama University Medical School, 2-5-1 Shikata-cho, Okayama, 700-8558, Japan

SOURCE: Diabetes Research and Clinical Practice, (October, 2000) Vol. 50, No. 2, pp. 109-115. print.

CODEN: DRCPE9. ISSN: 0168-8227.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002

AB Prescription of aerobic exercise for Type 2 diabetes mellitus (Type 2 DM) in clinical practice is frequently based on exercise intensity at maximum heart rate ($60 < \text{HRmax} < 79\%$), heart rate reserve ($50 < \text{HRreserve} < 74\%$), and rating of perceived exertion ($12 < \text{RPE} < 13$). We examined these parameters in Japanese males with Type 2 DM at ventilatory threshold (VT) to investigate the exercise capacity of Type 2 DM patients and re-evaluate the exercise prescription. Fifty-six Japanese Type 2 DM males without autonomic neuropathy (age, 53.5 ± 7.7 years; body mass index (BMI), 23.7 ± 3.6 kg/m²) were enrolled and compared with 56 age- and BMI-matched healthy Japanese males. VT was determined breath by breath during exercise test using a ramp protocol and rates of oxygen consumption (VO₂), work rate (WR), HR, DELTAHR, %HRmax, %HRreserve, and RPE were measured at VT. Type 2 DM patients had significantly lower VO₂ (3.6 ± 0.4 metabolic equivalents (METS)) and WR (62 ± 14 W) than controls (VO₂, 3.9 ± 0.6 METS; WR, 74 ± 13 W). %HRreserve, ($32.6 \pm 7.7\%$) was also significantly lower compared with controls ($37.6 \pm 8.3\%$), while %HRmax, was not different. RPE was also similar in diabetics (12.4 ± 1.5) and controls (12.9 ± 1.2), however, it was significantly lower in diabetic patients aged 60-69 years (11.8 ± 2.0) and those with distal symmetric sensory neuropathy (12.2 ± 1.0). Our results indicate reduced exercise capacity in Japanese Type 2 DM males and the exercise intensity of 60%HRmax, 30%HRreserve, and RPE 12 is recommended in elderly diabetics and those with diabetic sensory neuropathy.

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ACCESSION NUMBER: 2003151062 EMBASE Full-text

TITLE: Rationale and evidence for the use of oxcarbazepine in neuropathic pain.

AUTHOR: Carrazana E.; Mikoshiba I.

CORPORATE SOURCE: Dr. E. Carrazana, Neurosci., Clin. Devmt./Med. Affairs, Novartis Pharmaceuticals, Building 403, 59 Route 10, East Hanover, NJ 07936-1080, United States

SOURCE: Journal of Pain and Symptom Management, (1 May 2003) Vol. 25, No. 5 SUPPL., pp. S31-S35. .
Refs: 25
ISSN: 0885-3924 CODEN: JPSMEU

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 24 Apr 2003
Last Updated on STN: 24 Apr 2003

AB Oxcarbazepine is a second-generation antiepileptic drug (AED) with proven efficacy in managing partial epileptic seizures, with or without secondary generalization, in adults and children. The overlap between the underlying pathophysiologic mechanisms of some epilepsy models and neuropathic pain models supports the rationale for using certain AEDs in the treatment of neuropathic pain. Several AEDs have reportedly produced analgesia in a range of neuropathic pains, including painful diabetic neuropathy (PDN) and post-herpetic neuralgia. Increasing evidence suggests that oxcarbazepine can provide significant analgesia in several neuropathic pain conditions, including trigeminal neuralgia and PDN, and is also may be effective in treating neuropathic pain refractory to other AEDs, such as carbamazepine and gabapentin. The analgesic effects of oxcarbazepine, and its generally improved safety and tolerability profile compared with other standard AEDs, suggests that oxcarbazepine will be an important addition to the neuropathic pain armamentarium. The rationale and evidence to support the efficacy of oxcarbazepine are presented here. .COPYRGT. 2003 U.S. Cancer Pain Relief Committee. Published by Elsevier. All rights reserved.

L62 ANSWER 10 OF 10 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-26991 DRUGU T S Full-text

TITLE: Neuropathic pain: from mechanisms to treatment strategies.

Rationale and evidence for the use of oxcarbazepine in neuropathic pain.

AUTHOR: Carrazana E; Mikoshiba I

CORPORATE SOURCE: Novartis; Kissei

LOCATION: East Hanover, N.J., USA; Tokyo, Jap.

SOURCE: J.Pain Symptom Manage. (25, No. 5, Suppl., S31-S35, 2003) 1

Fig. 1 Tab. 25 Ref.

CODEN: JPSMEU ISSN: 0885-3924

AVAIL. OF DOC.: Neuroscience, Clinical Development and Medical Affairs, Novartis Pharmaceuticals, Building 403, Room 362, 59 Route 10, East Hanover, NJ, 07936-1080, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The use of oxcarbazepine in neuropathic pain is reviewed. Oxcarbazepine as a treatment for neuropathic pain including clinical evidence in trigeminal neuralgia, other neuropathic pain conditions and painful diabetic neuropathy are discussed. Oxcarbazepine is an effective and well tolerated treatment for neuropathic pain. This efficacy has been noted in a broad range of neuropathic pain conditions, including trigeminal neuralgia and painful diabetic neuropathy, and in patients refractory to other antiepileptic drugs, such as carbamazepine and gabapentin.

=> d his nofile

(FILE 'HOME' ENTERED AT 14:30:01 ON 24 MAY 2007)

FILE 'HCAPLUS' ENTERED AT 14:31:22 ON 24 MAY 2007

| | | | |
|----|--------------|--------|------------------|
| L1 | 1 SEA ABB=ON | PLU=ON | US20050215607/PN |
| | D ALL | | |
| L2 | 1 SEA ABB=ON | PLU=ON | US20050267195/PN |
| | D ALL | | |
| L3 | 2 SEA ABB=ON | PLU=ON | L1 OR L2 |

FILE 'REGISTRY' ENTERED AT 14:34:02 ON 24 MAY 2007

| | | | |
|----|--------------|--------|--------------------------------|
| L4 | 1 SEA ABB=ON | PLU=ON | 145375-43-5/RN |
| L5 | 1 SEA ABB=ON | PLU=ON | 207844-01-7/RN |
| L6 | 1 SEA ABB=ON | PLU=ON | MITIGLINIDE/CN |
| L7 | 0 SEA ABB=ON | PLU=ON | MITIGLINIDE CALCIUM HYDRATE/CN |
| L8 | 2 SEA ABB=ON | PLU=ON | (L4 OR L5 OR L6) |

FILE 'HCAPLUS' ENTERED AT 14:35:34 ON 24 MAY 2007

| | | | |
|-----|--------------------|--------|--|
| L9 | 97 SEA ABB=ON | PLU=ON | L8 OR MITIGLINIDE CALCIUM HYDRATE/OBI |
| L10 | 87 SEA ABB=ON | PLU=ON | MITIGLINIDE/OBI OR MITI/OBI(W)GLINIDE/OBI |
| L11 | 108 SEA ABB=ON | PLU=ON | L9 OR L10 |
| L12 | 3944 SEA ABB=ON | PLU=ON | DIABET?/OBI (L) (PROGRESS?/OBI OR COMPLICAT
?/OBI) |
| L13 | 2160940 SEA ABB=ON | PLU=ON | (INHIBIT?/OBI OR HINDER?/OBI OR IMPED?/OBI
OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR PREVENT?/OBI OR
BLOCK?/OBI OR ELIMINAT?/OBI) |
| L14 | 1486 SEA ABB=ON | PLU=ON | L12 AND L13 |
| L15 | 1486 SEA ABB=ON | PLU=ON | L12 (P) L13 |
| L16 | 3 SEA ABB=ON | PLU=ON | L10 AND L15 |
| | D SCAN | | |

FILE 'STNGUIDE' ENTERED AT 14:39:04 ON 24 MAY 2007

FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007

| | | | |
|-----|-------------------------|--------|---|
| L17 | 3 SEA ABB=ON | PLU=ON | L11 (P) L12 |
| L18 | 0 SEA ABB=ON | PLU=ON | L17 NOT L16 |
| | E DIABETS+PFT,OLD,NT/CT | | |
| L19 | 110617 SEA ABB=ON | PLU=ON | DIABET?/OBI |
| L20 | 54 SEA ABB=ON | PLU=ON | L11 AND L19 |
| L21 | 28 SEA ABB=ON | PLU=ON | L13 AND L20 |
| L22 | 28 SEA ABB=ON | PLU=ON | L13 (5A) L20 |
| | D KWIC 1-5 | | |
| | D L22 TI 1-5 | | |
| L23 | QUE ABB=ON | PLU=ON | AY<2004 OR PRY<2004 OR PY<2004 OR MY<2004
OR REVIEW/DT |
| L24 | 17 SEA ABB=ON | PLU=ON | L22 AND L23 |
| L25 | 3 SEA ABB=ON | PLU=ON | L10 AND L12 |
| L26 | 17 SEA ABB=ON | PLU=ON | L24 OR L25 |
| L27 | 271 SEA ABB=ON | PLU=ON | HYPERGLYCEM?/OBI (3A) (POST/OBI(W)PRANDIAL/
OBI OR POSTPRANDIAL/OBI) |
| L28 | 3 SEA ABB=ON | PLU=ON | L11 AND L27 |
| | D TI 1-3 | | |
| L29 | 13237 SEA ABB=ON | PLU=ON | HYPERGLYCEM?/OBI |
| L30 | 13237 SEA ABB=ON | PLU=ON | L27 OR L29 |
| L31 | 7 SEA ABB=ON | PLU=ON | L11 AND L30 |
| L32 | 7 SEA ABB=ON | PLU=ON | L28 OR L31 |
| L33 | 24 SEA ABB=ON | PLU=ON | L32 OR L24 |

10/519155

SAVE TEMP L33 FIN155HCAP/A
E MIKOSHIBA I?/AU
L34 15 SEA ABB=ON PLU=ON "MIKOSHIBA IMAO"/AU
E SUZUKI H?/AU
L35 328 SEA ABB=ON PLU=ON SUZUKI HISAO/AU
E KIYONO Y?/AU
L36 9 SEA ABB=ON PLU=ON KIYONO YUJI/AU
L37 346 SEA ABB=ON PLU=ON (L34 OR L35 OR L36)
E KISSEI PHARMACEUTICAL/CO, PA, CS
L38 673 SEA ABB=ON PLU=ON ("KISSEI PHARMACEUTICAL"/CO OR "KISSEI PHARMACEUTICAL"/PA OR "KISSEI PHARMACEUTICAL"/CS OR "KISSEI PHARMACEUTICAL CO"/CO OR "KISSEI PHARMACEUTICAL CO LTD"/CO OR "KISSEI PHARMACEUTICAL CO LTD"/PA OR "KISSEI PHARMACEUTICAL CO LTD"/CS OR "KISSEI PHARMACEUTICAL CO LTD CENTRAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO LTD CENTRAL RESEARCH LABORATORIES HOTAKA 399 83 JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD JAPAN"/PA OR "KISSEI PHARMACEUTICAL CO LTD NAGANO 399 8304 JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD PHARMACEUTICAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO LTD PHARMACEUTICAL RESEARCH LABORATORIES NAGANO 399 8304 JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD SHINSHU UNIVERSITY"/CO OR "KISSEI PHARMACEUTICAL COMPANY"/CO OR "KISSEI PHARMACEUTICAL COMPANY LIMITED"/CO OR "KISSEI PHARMACEUTICAL COMPANY LTD"/CO OR "KISSEI PHARMACEUTICAL INDUSTRY CO LTD"/CO OR "KISSEI PHARMACEUTICAL JAPAN"/PA OR "KISSEI PHARMACEUTICAL JAPAN"/CS)
L39 722 SEA ABB=ON PLU=ON KISSEI PHARMA?/PA, CS, CO
L40 722 SEA ABB=ON PLU=ON L38 OR L39
L41 8 SEA ABB=ON PLU=ON L37 AND L40
L42 6 SEA ABB=ON PLU=ON L41 NOT L33
SAVE TEMP L42 FIN155HCAAU/A

FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007

L43 84 SEA ABB=ON PLU=ON L8
L44 172 SEA ABB=ON PLU=ON L10
L45 10 SEA ABB=ON PLU=ON MITIGLINIDE CALCIUM HYDRATE
L46 173 SEA ABB=ON PLU=ON (L43 OR L44 OR L45)
L47 110 SEA ABB=ON PLU=ON L46 AND (L19 OR L27 OR L29)
L48 46 SEA ABB=ON PLU=ON L47 AND L23
L49 33 SEA ABB=ON PLU=ON L48 (P) L13
D TRIAL 1-5
SAVE TEMP L49 FIN155MULTI/A
L50 27 SEA ABB=ON PLU=ON MIKOSHIBA I?/AU
L51 22092 SEA ABB=ON PLU=ON SUZUKI H?/AU
L52 34 SEA ABB=ON PLU=ON SUZUKI HISAO/AU
L53 2 SEA ABB=ON PLU=ON KIYONO YUJI/AU
L54 63 SEA ABB=ON PLU=ON L50 OR L52 OR L53
L55 2 SEA ABB=ON PLU=ON L50 AND L52 OR L53
L56 2 SEA ABB=ON PLU=ON L54 AND L46
L57 2 SEA ABB=ON PLU=ON L55 OR L56
L58 6 SEA ABB=ON PLU=ON L54 AND (L19 OR L27 OR L29)
L59 6 SEA ABB=ON PLU=ON L57 OR L58
D L59 TI 1-6
L60 6 SEA ABB=ON PLU=ON L59 NOT L49
SAVE TEMP L60 FIN155MULAU/A

FILE 'STNGUIDE' ENTERED AT 15:06:18 ON 24 MAY 2007

D QUE L33
D QUE L49

10/519155

FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 15:07:58 ON 24
MAY 2007

L61 49 DUP REM L33 L49 (8 DUPLICATES REMOVED)
 ANSWERS '1-24' FROM FILE HCAPLUS
 ANSWERS '25-42' FROM FILE MEDLINE
 ANSWERS '43-45' FROM FILE EMBASE
 ANSWERS '46-49' FROM FILE DRUGU
 D L61 1-24 IBIB ED ABS HITIND
 D L61 25-49 IBIB AB IND
 D QUE L42
 D QUE L60
L62 10 DUP REM L42 L60 (2 DUPLICATES REMOVED)
 ANSWERS '1-6' FROM FILE HCAPLUS
 ANSWER '7' FROM FILE MEDLINE
 ANSWER '8' FROM FILE BIOSIS
 ANSWER '9' FROM FILE EMBASE
 ANSWER '10' FROM FILE DRUGU
 D L62 1-6 IBIB ABS
 D L62 7-10 IBIB AB

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